83

MEDICAL RECORD

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Vol. 161, No. 3

in weight reduction— new evidence of the efficacy of Dexedrine

Excerpts from a recent study entitled, THE MECHANISM OF AMPHETAMINE-INDUCED LOSS OF WEIGHT: A Consideration of the Theory of Hunger and Appetite —by Harris, S. C.; Ivy, A. C., and Searle, L. M.: J. A. M. A. 134:1468 (Aug. 23) 1947.

experiment 1. Does 'Dexedrine' Sulfate, by controlling appetite, decrease food intake and body weight in human subjects?

results ". . . our obese subjects lost weight when placed on a diet which allowed them to eat all they wanted three times a day . . ."

experiment 4. Does the rather prolonged administration of Dexedrine cause any evidence of disturbance of tissue functions?

results "No evidence of toxicity of the drug as employed in these studies was found . . . no evidence of deleterious effects of the drug was observed."

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* T.M. REG. U.S. PAT. OFF.

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An exciting new series of thirteen transcribed dramas on mental health, The Tenth Man, recently released by the National Mental Health Foundation, is now available for sponsorship on local radio outlets or for other educational uses. The programs in this series have received commendation and endorsement from the Group for the Advancement of Psychiatry and the United States Public Health Service.

Designed as tools for local mental health societies, doctors, social workers and others who wish to inform the public about psychiatric facts, these fifteen-minute radio plays dramatize some of the problems of the one man in ten who needs or will need professional care for a mental or nervous disorder.

Individual programs demonstrate how mental disorders can often be traced to lack of parental understanding in bringing up children and in some instances to marital difficulties. One program illustrates the therapeutic value of community centers for older people, particularly as they contribute to mental health. Other programs dramatize: the shocking admission procedures to which many mental patients are still subjected; the difficulties of the ex-mental patient in readjusting to his home and finding a job; the contribution of occupational therapy; the need for better psychiatric facilities; and what the concerned citizen can do to promote mental health in his community.

In resolving the various problems posed, appropriate community agencies, best-equipped to offer sound guidance, are either brought into the dramatization or suggested. Each program attacks old-fashioned ideas about mental illness, and suggests more up-to-date, understanding attitudes. There is a special stress on the fact that mental illness is no disgrace, but an illness, requiring prompt medical care.

Last year the Foundation produced its first transcribed series of eight programs, entitled *For These We Speak*, which has been broadcast on over 200 radio stations in the United States and Canada. This series received a citation in May, 1947 at the Ohio State Institute for Education by Radio, "in recognition of its outstanding educational value and distinguished radio production".

These programs have been widely heard, not only by radio audiences, but also by students in psychology classes, members of civic groups at public meetings, and employees in orientation courses at mental hospitals.

Organizations interested in securing radio sponsorship of *The Tenth Man* in their communities, or wishing to procure transcriptions for educational activities of a non-broadcast nature, may obtain further information by writing to: National Mental Health Foundation, 1520 Race Street, Philadelphia.

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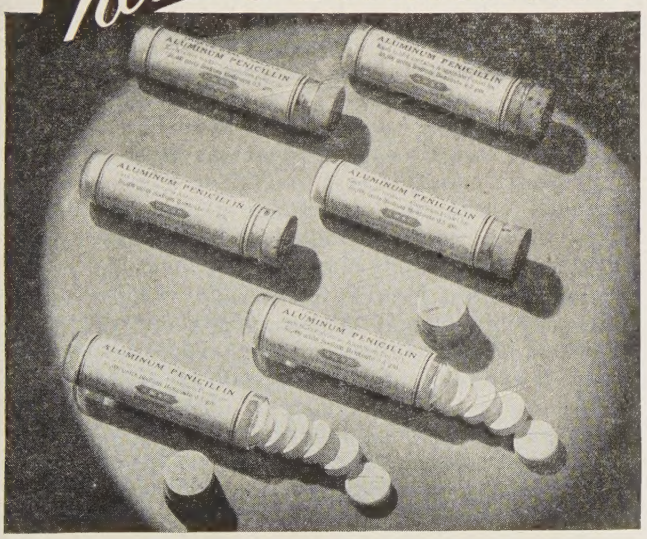

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Open Forum

MYSTERIOUS GERM DESTROYERS

T. SWANN HARDING
Falls Church, Va.

Streptomycin is merely the latest of the wonder drugs that is produced by molds and other lower organisms. It is common now to call some of them antibiotics, and they are used for the treatment of human infections. Streptomycin is the discovery of a little Russian immigrant who did excellent work in soil science for some thirty years of comparative obscurity at the New Jersey Agricultural Experiment Station. His name is Selman A. Waksman. He is a small vivacious man with a shock of graying hair and an iron-gray mustache.

He works in laboratories provided by various acts of Congress since 1862. The first of these made grants of public lands to the various States which were to sell them and to use the proceeds to found and support agricultural or "land-grant" colleges. Others made grants-in-aid to the States, which the States much more than matched, to be used for the performance of research in the field of agriculture. Waksman works on the experiment station staff and in the typical austere land-grant college laboratory and building—a purely functional structure throughout.

To Waksman a hundred thousand dollars is big money. When some waggish reporter discovered the word "antibiotic" in the President's budget message and remarked that it was obviously a $440,000-word, if so much were to be spent in research on the subject, Waksman modestly wished he had just a quarter of that sum—not for himself—but to plow back into research on streptomycin and related substances. Waksman is without vanity, affable, and fortunately possessed of a robust streak of humor.

He has no desire whatever to become a high-salaried, high-pressure expert for any of the commercial drug companies which have made him flattering offers. While private enterprise is currently investing millions of dollars in plants to manufacture his drug, he would like to see a public patent granted on it with royalties on that put back into more research.

Above all he wants to do more planned research right where he is, but it seems that the American way, with celebrities, threatens to end his way of life altogether. Invitations to speak everywhere swamp him at the rate of one a day, many of them imperative wires asking him to come two thousand miles to deliver a six-minute talk—always on streptomycin.

No meeting, dinner, banquet, or chamber of commerce function is complete without him. The radio demands him; interviewers and photographers intimidate him.

So he finds it all but impossible to plan and carry out his research projects anymore, yet there is so much more to be done. His natural affability tends to make him accessible to celebrity hunters. But he does see the irony of it all and looks back with nostalgia to the quiet time in the past when he could pursue his study of soil organisms unmolested. But what is streptomycin? What does it do? How does it fit into therapy? For that matter, what is an antibiotic—a word Waksman coined?

Essentially it is a substance which deprives something else of bios, or life. Like the sulfa drugs, penicillin, and salvarsan, streptomycin kills germs of certain kinds. There is nothing so very new about this. Pasteur, in 1877, observed that some germs killed other germs and, in 1896, Gosio recorded that a mold on which he was working produced a substance that would kill bacteria. In fact he obtained a germ-killing crystalline compound from one of the many penicillin molds, while studying moldy maize.

All of this comes under the older term chemotherapy, the treatment of infections with chemical compounds, as Paul Erhlich learned how to treat syphilis with arsephenamine or salvarsan in 1910.

Then, in 1935, Domagk discovered that a certain dye with a long name, which later came to be known commercially as "prontosil", would deal death to the kind of streptococci which dissolve red blood corpuscles. A little later others found that the part of the molecule containing the dye could be dispensed with, and thus sulfanilamide came into use.

Gradually its various relatives, sulfapyridine, sulfathiazole, and sulfadiazine were developed and put to work against certain infections for which each proved best. But all these drugs tend to have unfortunate side reactions from time to time.

Then, as is now well-known, Fleming in 1929 observed that when the mold Penicillin notatum fell into a culture of staphylococci it killed the germs. The mold itself did not do that, but some substance the mold produced. This was found, purified, crystallized, and called penicillin. In 1945 alone a hundred million dollars worth of it was made. Its mass production at a reasonable price was made possible by research at the Department of Agriculture's Regional Research Laboratory, at Peoria, Ill. It killed many germs without producing undesirable side reactions on patients.

However, the search continued for more and better antibiotics and Waksman was one of these searchers. Being a soil scientist he naturally wondered if any soil organisms produced useful antibiotics. So he tested hundreds of them on hundreds of media to see whether any of them could be induced to manufacture a germ killer. Meanwhile it was found that a soil bacterium called Bacillus brevis, first apprehended in the sewers of Berlin, did produce a substance that would kill germs.

Tests of it and related strains of bacteria enabled Waksman and his associates to produce two powerful antibiotics in 1941-42, but they both had powerful toxic actions on animals and had to be set aside for further study.

Turning to another group of soil organisms with

the formidable name actinomycetes, Waksman and his associates were more successful. In 1944 they discovered how to produce streptomycin which was found, on injection, to destroy many bacteria which resisted penicillin and the sulfa drugs. It also appeared to produce no serious or uncontrollable side effects. Waksman became a celebrity.

What is the real status of his discovery today? The soil microorganisms have long been a rather neglected group, with their study being confined to a few agricultural specialists. Nevertheless Waksman eventually found that a fifth of those he tested proved capable of manufacturing substances that would kill bacteria. But, the antibiotics were not a natural part or product of the soil organisms, which merely produced them when grown on certain culture media.

Moreover both the soil organisms and the antibiotics come in wide variety, and some of the organisms produce substances quite different from antibiotics. Some of the antibiotics produced are active against all sorts of bacteria, some are highly selective and will kill off only one or two varieties, and some kill fungi. Many of them are quiet poisonous. But the production of the antibiotic is more a function of the culture medium than of the soil organism.

Again, a micro-organism must sometimes be tested on as many as a hundred or more different culture media before it produces anything resembling an antibiotic. So it is the cultural environment, not the strain or organism, which determines what the antibiotic will be like. Some organisms have never produced anything at all, though they have been grown in the laboratory for more than thirty years on all sorts of media. Some will produce richly on one medium and not at all on another. Finally, streptomycin may be produced by a number of wholly different organisms.

The fact that so many different antibiotics can be produced points the way to future research. Obviously it is necessary to discover just as many of these substances as possible, to make intensive search for those which kill bugs resistant to agents now known, and to seek out others that will kill viruses, which would be extremely valuable.

Waksman believes the search has just begun. He wants to find antibiotics with widespread killing power, others so highly specific that they will track down every single germ of a certain kind in the body and destroy it, all preferably without bad side effects on patients.

It is rather curious, also that no one knows exactly how antibiotic agents kill germs, and it is fundamentally important to find that out. No one knows why antibiotics can be so lethal to certain bacteria and yet prove harmless to the body's living cells. No one knows whether their action is principally chemical or physical, or how deeply it may be lodged in the structure of molecules.

Most significant is the fact that strains of germs which are originally killed easily by an antibiotic may soon build up such resistance that it can no longer destroy them. This is true to some extent

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of penicillin and the sulfa drugs, but they are generally used in attacks on acute infections and the germs have little time to build up resistance. Streptomycin is being tried extensively on chronic infections like tuberculosis and undulant fever. This gives the germs plenty of time to develop and fortify their resistance.

In any group of a hundred million germs there are possibly five hundred which will resist an antibiotic, no matter how strongly it is used. The job is to find antibiotics that will kill organisms of all degrees of resistance. Different bacteria also develop resistance at different speeds. How do they do this? Again no one knows, but there are hypotheses.

Possibly the antibiotic selectivity kills off the germs of low resistance, thus permitting the highly resistant survivors to develop a very robust strain. That takes time but it could be done. Or maybe it is all just a matter of genetics. New strains of the germ may arise spontaneously, as sports, and rapidly reproduce. Or maybe the germs have alternative mechanisms of survival. If the primary one breaks down because of the action of a certain antibiotic, secondary ones come into operation and the germ learns how to live in the presence of a substance that might otherwise destroy it.

Possibly the antibiotic selectively kills off germs that are susceptible and the survivors spontaneously develop renewed strength. Many highly complex problems remain to be solved. No wonder Waksman wants time and money to perform more research. Certainly he does not regard streptomycin as a panacea.

Just recently doctors attending a medical meeting in New York warned against the indiscriminate use of the drug, even by physicians, and laymen should never use it without medical supervision, of course. For one thing the substance is not always prepared in pure form and improved purification methods are needed. Much of the publicity about it, which no scientist like Waksman would issue, has been premature, misleading, and has aroused false hope. So many writers find it profitable to sell "hope-for-sufferers-from-soandso" articles.

The fact is that streptomycin does have demonstrable toxic effects when administered over long periods. But it is effective against about half of the objectionable organisms surgeons meet up with. Yet bacteria do rather quickly learn to resist it and, if given indiscriminately, it might soon altogether lose effectiveness, just as penicillin may if similarly abused.

Providing the organisms causing the condition happen to be the kind that streptomycin destroys, the drug gives excellent results in infections of the urinary tract, in some cases of peritonitis, in gonorrhea, and in some dysenteries and septicemias or blood poisonings. It does not help infections of the bones or of the prostate gland and is of little value in typhoid. It arrests undulant fever, is good in meningitis, and excellent in tularemia or rabbit fever. It also gives excellent results in direct application.

Results in the treatment of tuberculosis are as yet so uncertain that no valid conclusions can be drawn. Much more work must be done.

Some of the drug's toxic side effects are due to impurities. The most serious of these are so far found is an irreversible change that takes place in the eighth cranial nerve, if streptomycin be taken too long or in too large quantities. This adversely affects the sense of balance, causing dizziness, nausea, and partial deafness. In certain circumstances streptomycin can also injure the kidneys.

That is about all that can be said with certainty. Research workers like Waksman have high ethical standards and unassailable integrity. They are not to blame for the distorted publicity of and the abuses to which their discoveries are subject by the unscrupulous. That's just an old American custom, like that of transforming serious research investigators into celebrities, and then trying to monopolize their time and attention so much that they find it all but impossible to continue their studies.

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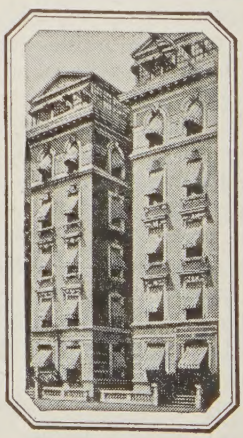

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World Health Assembly Will Meet In Geneva

The World Health Assembly, representative of all members of the World Health Organization, will be convened in Geneva on June 24, 1948, under a recent decision made by the Interim Commission, officials of the State Department announce. This will be the first meeting of the annual Assembly and will be largely concerned with the development of the initial program of the World Health Organization.

At present, 22 Members and 8 non-members of the United Nations are parties to the Constitution of WHO. As the Constitution does not legally come into force until 26 Members of the United Nations become parties to it, it is hoped that additional nations, including the United States, will join the Organization prior to the June Assembly.

If the Assembly follows the recommendations made by the Interim Commission, WHO will focus its activities during the early years on Malaria, Tuberculosis, Venereal Diseases, and Maternal and Child Health. At the same time, it will continue important functions in the control of international spread of disease, which it has inherited from the League of Nations and the International Office of Public Health at Paris.

Paramount attention will be focused on a global anti-tuberculosis program, which will include intensified research and assistance to Governments in TB control. Figures which say that four to five million people, according to conservative estimates, die of TB each year, and that ten times as many are infected, do much to justify the initiation of this far reaching program.

In order to eliminate this disease the WHO. IC Expert Committee agreed that a systematic campaign should be waged along the following lines: 1. Prevention, 2. case finding, 3. isolation and medical care, 4. rehabilitation and after-care, and 5. social and economic protection to afflicted families.

At the Fifth Session of the WHO Interim Commission in January and February measures for active cooperation with the ICEF in its program to vaccinate 15,000,000 children and adolescents already had been discussed.

The greatest contribution which the WHO can make in the field of TB research, the Committee decided, would be by developing and recommending uniform procedures. Principal problems on which such action is needed are: 1. Tuberculin and tuberculin testing; 2. Preparation and clinical use of BCG; 3. Classification of tuberculosis; 4. X-ray interpretation and mass radiology; 5. Laboratory diagnosis of tubercle bacilli, and 6. Evaluation of new chemotherapeutic agents such as streptomycin. In this connection, the Committee recommended that a streptomycin conference be called early in May in the United States.

Also scheduled for the June meeting is the taking up of Ethiopia's staggering health problems, particularly a venereal disease rate estimated as high as 80 percent in some areas. Dr. N. Goodman, director of field services for WHO. IC has been

(Continued on page 140)

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studying in Addis Ababa the works of Greek, Canadian, British, and the United States public health specialists who have been operating in Ethiopia since the first of last year, when the program was transferred from UNRRA to WHO.IC.

The health authorities now in that country will access the extent of the TB and VD problem among the 12 to 15 million people of Ethiopia and advise the Health Ministry on methods of combatting the diseases.

Medical awareness in that country has been forwarded by the recent showing of health films in schools and which are also shown to the personnel of the Ministry of Health.

The WHO chief nurse has taken a leading part in re-establishing the Ethiopian Red Cross, which works closely with the Ministry. She has also organized a Red Cross course in home care of the sick for Ethiopian volunteer workers.

In Italy a large scale anti-malaria campaign during 1948 and 1949 is now being shifted into high gear due to the recent arrival of 300 tons of DDT. In addition to the fight against malaria, WHO.IC medical liaison officers are assisting the Italian health authorities in tuberculosis control, in the rehabilitation of port sanitation services, in programs for maternal and child care, in working out details for the construction of a penicillin plant, as well as in many other fields.

Dr. Meyer Perlstein Discusses Cerebral Palsy In Latest Booklet

Latest medical knowledge on the causes and treatment of cerebral palsy is contained in *The Problem of Cerebral Palsy Today*, Dr. Meyer A. Perlstein's new 57-page booklet distributed by the National Society for Crippled Children and Adults, Chicago.

Prepared with the assistance of William McPeak, prominent social science analyst, Doctor Perlstein has written this booklet as an aid to the medical profession, for leaders in community organizations, and as a guide to workers in the fields of health and rehabilitation.

The contents include a description of the problem of the cerebral palsied child, a suggested state program, professional training, research needs, and cerebral palsy as a socio-economic problem. Of special interest are sections devoted to an expanded diagrammatic chart of how a model cerebral palsy program operates, and some hypothetical case histories illustrating the mechanics of the cerebral palsy program.

* * *

Hodara's disease, or trichorrhexis nodosa of women of Constantinople, is named after Menahen Hodara, who described the bacillus multiformis of trichorrhexis.

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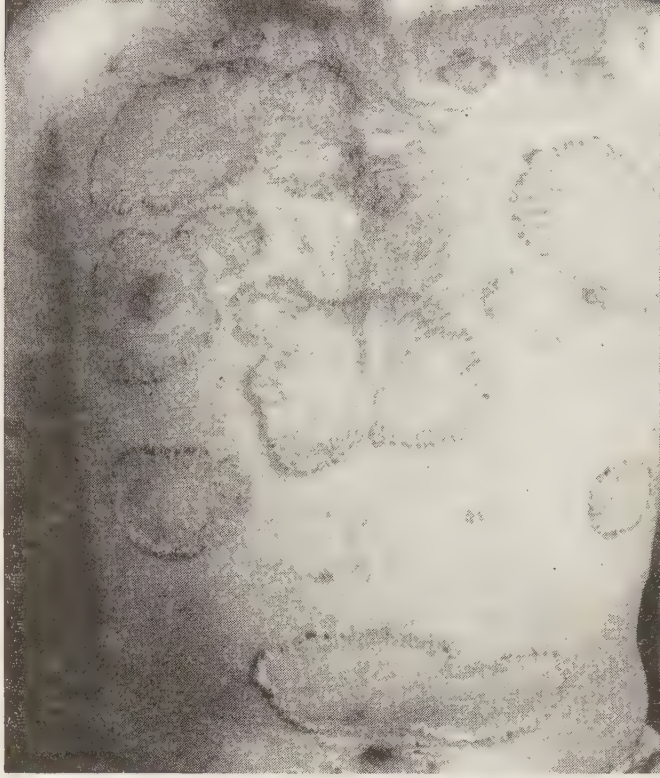

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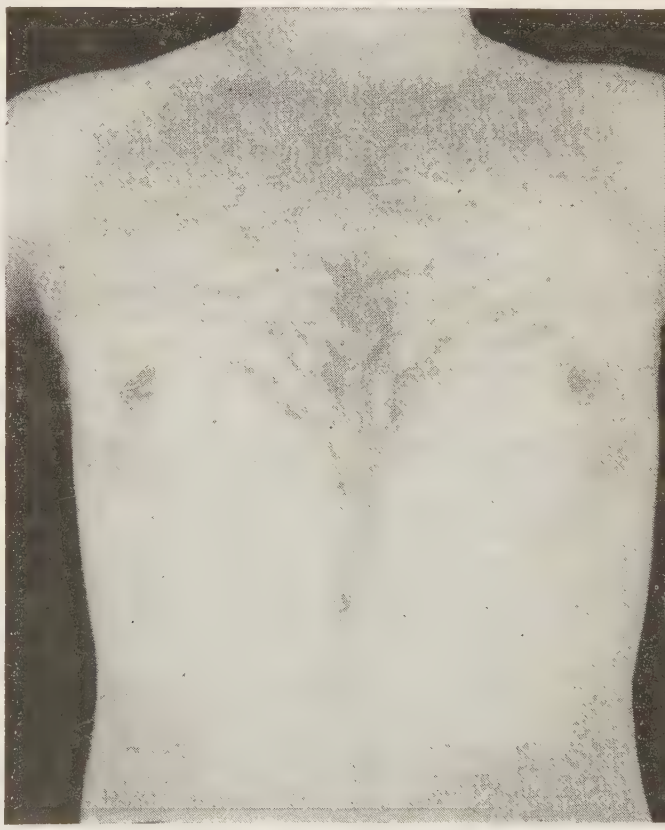

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RIASOL for PSORIASIS

Critique

Lukutate: Who remembers this tropical fruit-food so widely advertised in the very best magazines, such as *Harper's* back in 1929? Said an advertisement clipped from this worthy magazine, October, 1929—the time of the great stock decline: "Physicians and scientists attribute the invigorating qualities of Lukutate to rare vitamins or mineral elements. The very name Lukutate means *comeback*. It stores up energy for the rapid pace of modern business and social activities." The medical authorities in Germany and Austria had then already stopped sale of Lukutate as a swindle. Hiller, its manufacturer, was a well-known patent medicine man. He had doctors in his pay writing dissertations about the stuff and how the East Indians used this wonderful berry to invigorate them. But when Hiller was asked to produce the plant he couldn't. Yet he had Europe posted with Indian landscapes and beautiful Indian girls when he was compelled to clear out over night because his bubble burst through exposure. Actually he got a count, down on his uppers, to write a long article proving that elephants lived a sexually active life for a century by being fed this berry. Lukutate was a sort of concentrated blackberry marmalade, and Hiller made lots of money and got plenty of spontaneous endorsements even from American physicians. At the very same time the natives of East India were industriously scouring Europe in the effort to discover and appropriate rejuvenators and aphrodisiacs!

The "mouth parts" Some years ago a popular antiseptic advertised using a spectacular drawing of the human being captioned "80 square inches inside your mouth where germs of 30 diseases start." You were to use the antiseptic and end those germs. Actually the "mouth parts", as drawn, extended from the lips into the mouth itself and down the throat to the first rib! Of the 30 diseases supposed by the advertiser to start in this area only one certainly did so, parotitis; the other 29 diseases the advertiser glibly named started elsewhere. Moreover there are not more than 50 square inches of tissue from the lips to the epiglottis. Finally, if the antiseptic were, as advertised, strong enough to cleanse the mouth of germs in one minute, it could only have done so by burning out the entire mucous membrane!

1929 incomes At the very height of prosperity in 1929, and just before the big market break, the Bronx Committee of the New York Tuberculosis and Health Association obtained data, through trained social workers, on 501 representative families and one-third of them had less than $35 a week to live on, while more than three-fourths of them had less than $50 a week. At least 7 percent were in poverty and dependence, 26 percent could barely maintain themselves, 45 percent lived better but could afford neither savings nor luxuries, and 8 percent only had a surplus over their living expenses. In that period a family on less than $1,440 annually was classed as in poverty, for that sum provided bare maintenance and allowed only $25 per family per year for drugs and medical care! An annual family income of $2,150 implied health and decency standards, not comfort, and allocated $75 a year for medical attention for the family. Bare comfort could be attained on $3,240 per family per year for an industrial worker and $3,670 for a professional and, in this case, $200 a year could be allowed to meet the family's doctor, dentist, and druggist bills.

Pharaoh's heart You have no doubt read somewhere that Pharoh's heart was hardened against the Isrealites, and it was, no mistake about that—it was as hard as a rock. The heart was examined some quarter century ago by S. G. Shattock of the Royal College of Surgeons —"Mr." Shattock, as they have it in England. He was able to dissect the aorta and compare with the heart of a man recently dead. They were so similar no pathologist could tell the difference, both being atheromatous. The arterial system was rigid and, it was said, mental rigidity necessarily accompanied it. The *Book of Exodus* offers proof. The wrappings were first removed from this mummy of Pharoh Menephtah, the ruler during the oppression, on July 8, 1907. The mummy was found in the tomb of Amenophis II in the Valley of the Tombs of the Kings at Thebes, and Elliot Smith, professor, found the body incrusted with crystals of common salt. Thereupon the inevitable wag who was present remarked: "There you see the confirmation of the Red Sea episode." But Professor Smith also observed calcified patches on the aorta.

Five-day week In the *North American Review* for November 1929 you will find an article by John J. Raskob telling the exciting news that the five-day week has already entered many industries and that well-paid workers with good environmental conditions produce as much in five or five and one-half days as they did in six. Raskob predicted the universal adoption of the five-day week by industry to give workers time and opportunity to function better as consumers. He felt that production was already geared up to such a speed that attention must be concentrated on improving consumption. He said that our industrial machinery then needed "further adjustment toward increasing the worker's share of ownership and profits, and endowing him with more time to use and enjoy the products." Unless workmen had time to spend their money, overproduction was bound to sink us. Today's inflation, of course, makes money spending a minor chore, if not a pleasure; you are soon done with it in any case.

Food and polio Now Professors Paul F. Clark and Conrad Elvehjem of the University of Wisconsin have come forth with evidence that diets lacking certain vitamins and/or minerals, or other nutritional factors, tend to inhibit the course of poliomyelitis *in mice*. Paralysis in mouse polio has been altered or prevented by restricting the intake of vitamin B-1, potassium, phosphorus, and tryptophane, but this does not destroy the virus in the body. Eating moderately appears to be beneficial for mice affected with the disease; the same thing has proved true in cancer and in longevity research. Maybe something to help human sufferers will come from this in time.

Saskatchewan hospitals An expenditure of $3,301,571 was shown for the first 6 months of 1947 on the Saskatchewan Hospital Plan, of which $3,007,884 went for hospitalization and $293,687 for administrative expenses, while hospitalization tax collections during this period totaled $3,519,355, and there was nearly ten thousand in miscellaneous revenue. During this period there were accounts for 54,817 adults and children and 9,937 new-born infants were discharged, while there was accrued expense, of course, for patients already in the hospital. Since the population covered was 780,445, the annual rates, new-borns omitted, ran 140 persons hospitalized with 1,434 days of care per 100,000 of population, the average individual stay in the hospital being 10.2 days.

Home cooking Home cooking has messed up a lot of food. In fact some women have a positive genius for turning good food into bad in the kitchen, depriving it of all succulence, taste, and nutritive value in the process. It is not the proteins, carbohydrates, vitamins, and minerals in the foods as purchased that are of most interest to us, but those the housewife manages to convey to the dining tables. Recently four specialists of the U. S. Bureau of Human Nutrition and Home Economics reported on studies of the Vitamin and Mineral Content of Certain Foods as Affected by Home Preparation. They started out with a preliminary study of 20 foods—vegetables, meats, poultry, breads, and cereals, and then made a more extensive study of potatoes, carrots, and peas. The effects of cooking were determined on the following nutrient elements: Ascorbic acid, dehydroascorbic acid, carotene, thiamine, nicotinic acid, riboflavin, ash, calcium, phosphorus, iron and moisture—though not for all foods in all cases. The standardized cooking procedures studied were boiling, baking, steaming, cooking in a pressure saucepan, simmering, braising, and frying. The report, Miscellaneous Publication No. 628 of the Department of Agriculture, is intended for research workers in nutrition and would be useful to physicians. It may be procured from the Department of the Superintendent of Documents, Government Printing Office, Washington, D. C.

THE CRITIC

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U. of Chicago Declares Importance of Penicillin Against Harmful Effects of Bacterial Poisons

Penicillin, apart from its ordinary therapeutic activity for infections, will also protect animals against the injurious effect of bacterial poisons, three University of Chicago physicians announced.

Writing on *Protection against Bacterial Endotoxins by Penicillin and Its Impurities,* in a recent issue of *Science,* Drs. C. Phillip Miller, Alden K. Boor and Walter D. Hawk also announce that the impure preparations of penicillin, containing an unknown substance, provide a much greater degree of protection than the pure crystalline penicillin.

The investigation, carried on in the laboratory on mice, shows that large doses of penicillin administered under the skin or into the abdomen will protect the mice against the lethal effect of a solution of killed bacteria. Penicillin is effective against meningococcus, gonococcus, paratyphoid A and B, dysentery bacillus, salmonella of food poisoning, and typhoid.

Injection of any one of the bacterial solutions produces a severe intoxication, fatal to the animal unprotected by penicillin.

The impure penicillin, an intermediate fraction in the commercial preparation of crystalline penicillin, plus 10,000 units of the crystalline, is five to ten times more effective than the crystalline penicillin alone.

Work on the identification of the unknown substance in the impure penicillin is being continued at the University of Chicago.

The research is being carried on under a grant from the antibiotics study section of the National Institute of Health of the United States Public Health Service.

Dr. Harvold To Direct National Cleft Palate Clinic In Norway

Dr. Egil Harvold, who has been appointed to set up a national cleft palate clinic in Norway for the free treatment of children, recently spent three months in the United States studying the research progress in the treatment of cleft palate cases at the Universities of Rochester, Harvard, Michigan and Iowa.

Dr. Harvold, whose full time job is instructor of orthodontics in the school of dentistry, Oslo, visited this country on a grant extended by the Norwegian government. While on the Iowa campus the doctor expressed special interest in the high degree of cooperation and quality of its four departments interested in cleft palate cases. All cases are interchanged through the departments of surgery, speech pathology, orthodontics and prosthetics.

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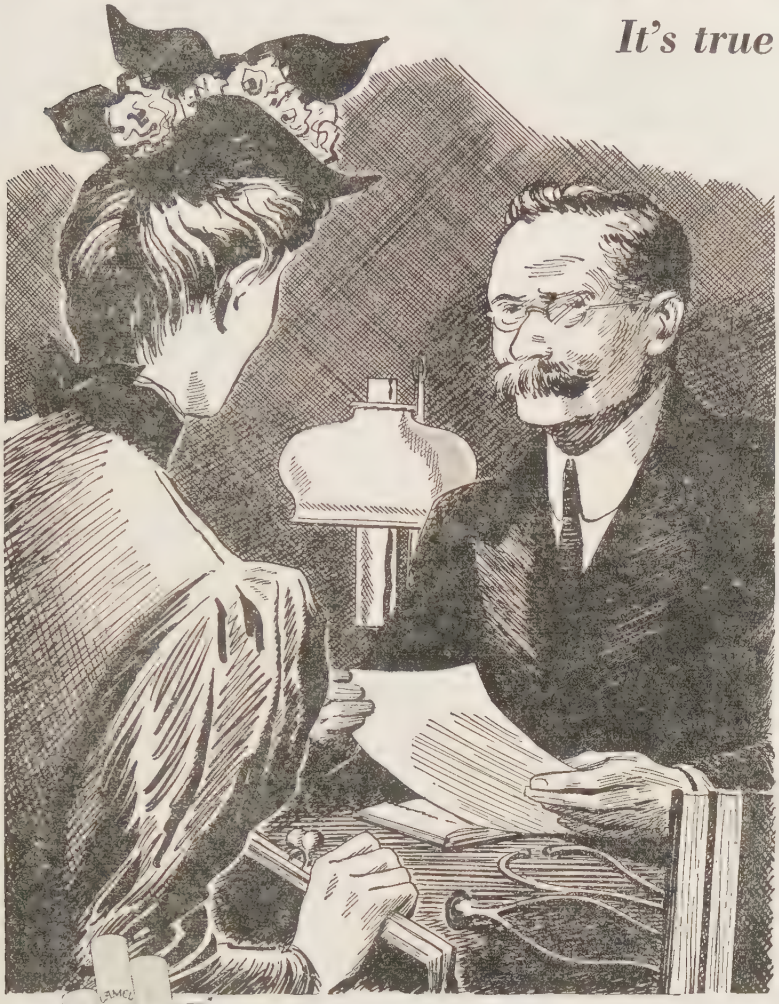

BALLANTYNE, in his early studies of anatomical and pathological conditions found in the new-born, sensed the value of routine prenatal care in obstetrics. As a pioneer for prenatal care he was the first to establish a clinic for the expectant mother. World-wide acceptance of Ballantyne's concepts quickly followed his successful experiences in prenatal supervision.

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That leaves the Average American (3) matched up with the Horn of Plenty (1).

As such an American, you'd like that to be true, wouldn't you?

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MORPHOLOGICAL AND BIOCHEMICAL CHANGES PRODUCED BY SULFONAMIDES

MICHELE GERUNDO, M. D., Ph. D.*

Honolulu

Experimental

During cultural experiments on fluid media it was seen that in many instances the bacteria growing on sulfasuxidine-containing media clumped and settled at the bottom of the tube leaving a clear supernatant fluid, or grew only on surface in a web-like or ring-like pattern. Considering the possibility that sulfonamide changed the morphological and biochemical characteristics of the bacteria, several species were grown on Russell Double Sugar Agar, containing 1:1000 sulfasuxidine.

In sulfasuxidine medium the typhoid bacillus showed granular colonies with polycyclic contours, resembling the rough type of this species. On ordinary medium the same strain showed a smooth type of colony. By picking the granular colonies and transplanting them on sulfasuxidine medium, as well as on ordinary tryptose agar plate, the sulfasuxidine plates showed again the same granularity, whereas the ordinary plates inoculated with same colonies showed a reversal to smooth colonies.

With *Salmonella schottmulleri,* however, no appreciable differences were seen between the two sets of plates.

In a second series of experiments eosin methylene blue agar plates were used without carbohydrates or in combination with different carbohydrates. On eosin methylene blue agar plates, containing lactose and sucrose, the presence of sulfasuxidine prevented the formation of metallic sheen which E. coli usually produces; at the most, only a dark-wine color was present. (Table I)

When the carbohydrate was excluded from the medium, no metallic sheen was apparent in either the sulfasuxidine containing plate or the control plates, suggesting that the production of the metallic sheen is due to metabolic products of carbohydrate fermentation. In table II growth, as well as production of metallic sheen are recorded for glucose, levulose and sucrose, incorporated separately in the medium. Paraaminobenzoic acid added to the medium antagonized the sulfasuxidine inhibition only to a certain extent, as in several instances, (Table III), plates containing sulfasuxidine and PABA failed to show the sheen which was instead evident in the control plates. (Table IV)

By adding glucose to the medium, sheen inhibition was noted with many more bacteria. *Eb. typhi,* which grows uninhibited by sulfasuxidine, lacked the sheen on eosin methylene blue plates containing the drug. (Table IV) The phenomenon seemed definitely linked with respiratory enzymes of the bacteria which were either delayed or inhibited by sulfonamides, or prevented from complete oxidation of the carbohydrates.

It was observed occasionally that after prolonged incubation some plates containing sulfasuxidine showed a small number of colonies with metallic sheen. On transplanting colonies without sheen on ordinary plates, the sheen was restored without delay.

The study of motility was followed by cultural, as well as ultramicroscopic methods. By using a motility medium it was seen that resistant strains, like *Eb. typhi* or *Aerog. Aerobacter,* were not affected at all, whereas more susceptible strains, like E. coli showed lack of motility.

Proteus vulgaris, which is among the more resistant bacteria, showed, at the first, partial diffusion in sulfasuxidine medium, but, on being serially transplanted on sulfasuxidine media, it lost its motility and also its spreading capacity. Paraaminobenzoic acid counteracted this sulfasuxidine action. The loss of motility, however, was not a permanent characteristic, as retransplanting on ordinary media restored this property.

* From the Department of Bacteriology, University of California and the Department of Laboratories, Hilo Memorial Hospital.

Table I

Eosin Methylene Blue Agar
Sulfasuxidine 1:500
Lactose and Sucrose Present

Bacteria	*With Sulfasuxidine*	*Without Sulfasuxidine*
A45 RS1 (1) (E. coli com.)	Moderate growth; no metallic sheen.	Good growth. Marked metallic sheen.
A45 RS2 (2) (E. coli com.)	Good growth. Only isolated colonies show metallic sheen.	Good growth. Metallic sheen.
Eberth. typhi S	Colorless colonies. No appreciable difference.	Colorless colonies from control.
E. coli communis (2) 10 from sulfasuxidine	Very few black colonies. Good growth. Rest colorless or wine red.	Very few black colonies. Good growth.
2295 (E. coli communis) (1)	Scanty growth. Few black colonies only at the end of the streak, the rest colorless.	Good growth. Uniform metallic sheen.
E. coli communior (2) 15	Moderate growth: only at the end of the streak few black colonies with no distinct metallic sheen.	Good growth with uniform distinct metallic sheen.
E. coli communis (2) 10	Scanty growth of small colorless colonies.	Good growth of large colonies with metallic sheen.

(1) freshly isolated.
(2) laboratory stock cultures.

Table II

Eosin Methylene Blue
Sulfasuxidine 1:500 (saturated solution)
Glucose, levulose, sucrose are added to the medium separately.

	WITH SULFASUXIDINE				WITHOUT SULFASUXIDINE			
Bacteria	*No sugar*	*Gluc.*	*Levul.*	*Sucr.*	*No sugar*	*Gluc.*	*Levul.*	*Sucr.*
B. Coli communior from sulfasuxidine	±	+(2)		+(0)	+±	+++(4)		++(0)
Salm. ab. ovis	+	+			+	++		
B. Coli communior	+(0)	+±(1)	++(1)	+(0)	++(0)	+++(4)	+++(4)	++(4)
229 S. (Coli communis)	+(0)		+(0)		++±(0)		+++(3)	
229 S from sulfasux.	?(0)				++(0)			
B. Coli communis 10	±(0)	+(1)	++±(1)		++(0)	++(4)	+++(4)	
B. Coli communis from sulfasuxidine	?(0)	++(2)	+±(3)		+	++(2)	+++(4)	
Pseudomonas 1 from sulfasuxidine		++				++		
A45 RS from sulfasux.		+(1)		+(0)		+++(4)		+++(4)
A45 RS after two subcultures in sulfasux.		+(1)	+±(1)			++(3)	+++(1)	
A45 RS				+(0)				+++(4)
Shig. alkal.			+(1)				++(4)	
Para B			++(1)				+++(4)	
Shig. dysent.			±(0)				+(0)	
Flexner			+(0)				+(1)	
Alkalig. 110			—				+++(0)	

The number in parenthesis after the sign of growth refers to the degree of metallic sheen.* B. coli communior, freshly isolated.

The dark-field study of motility has been conducted with a rather simple technique, by taking samples of growing bacteria at various intervals after inoculation into a suitable medium containing various sulfonamides, or by mixing directly on the slide growing bacteria with solutions of various sulfonamide compounds. Only preliminary findings can be given at this time, as this phase of the work is now being developed and any speculation on the findings would be premature. Under the dark-field, motility is affected rather promptly.

After an interval varying from 10 minutes to one hour in contact with sulfonamide many bacteria lose their motility. It is noticeable that immediately after mixing growing motile bacteria with sulfonamide, the motility seems apparently increased and changed in type, as if electrical charges were in action.

Finally, we may mention at this point that after a series of passages on sulfasuxidine containing media, a strain of Proteus vulgaris lost the property of splitting gelatin, whereas after same number of passages, Pseudomonas aeruginosa never lost its gelatinase. Para-aminobenzoic acid counteracted to a certain extent the sulfasuxidine inhibition of the gelatinase of Proteus vulgaris.

Discussion

Van Loghem (1) discussing the importance of the genetic conceptions in bacteriology, defined the phaenotypus

> . . . as the potential totality of the physiological and pathological reactions of an individual to the normal and abnormal stimuli from the outer world . . .

The study of genetics in bacteriology is hindered by the fact that we have an endless somatic division without apparent death of the parental body.

Van Loghem criticized the attitude of many bacteriologists who seek to gather information about genetics of bacteria by the study of colonies on artificial media. For him, a colony is the most unnatural type of growth and he strongly objects to new laboratory species being called mutants: more suitable names being regression, atrophy or mutilation.

Changes of clone, which he calls adaptates and fixates, are only responses to outer world; they must be studied on the basis of the multiplicity of substrates which form a living dynamic mosaic.

With this premise in mind perhaps a closer scrutiny of the literature and experimental data will serve to avoid again the easy tendency we have to speak about new species or mutants created inside the test tubes by the addition of few crystals of a magic substance to a particular medium.

McLeod and Daddi (2) found that *in vivo* and *in vitro* fastness of a pneumococcus type I was not associated with changes of morphology, virulence or specific immunologic characteristics. With the exception of a lack of formation of peroxide, the resistant strain showed the same growth and sugar fermentation as the non-resistant parental strains.

Sesler, Schmidt and Belden (3) found that strains of pneumococcus which had acquired a high degree of resistance to the sulfonamides, retained that resistance for an indefinite period, and that strains which had acquired only a moderate degree of resistance lost this characteristic after removal from contact with a sulfonamide.

Zahl, Hubner, and Cooper (4) found that a sulfonamide would attenuate the endotoxins of certain gram-negative bacteria, but their conclusions seem to rule out the possibility of a direct action upon antigenic structure.

McKinney and Mellon (5) succeeded in producing colony dissociation of pneumococci on glucose-blood agar plates, after having treated experimentally infected animals with sulfonamides. Small mucoid colonies, uncollapsed, with green reactive zone, changed, after sulfonamide treatment, to collapsed mucoid colonies with stippled surface or to dwarf colonies containing rod- or spindle-shaped organisms. There were, however, no changes in the exudate produced by the bacteria nor in virulence of the bacteria themselves. The authors assumed that there is an obvious interdependence between a diminished growth rate and the elaboration of a gradient of cultural phases. The sulfonamides act upon enzyme systems, which gradually disappear, as time exposure to the drug increases. Dwarf colonies seemed to originate from inhibition of certain of the bacterial metabolic activities, as they are implemented by the enzymes or "activation centers" of the bacterium. However, all of the changes were readily reversible on cessation of sulfonamide treatments.

Hadley and Hadley (6) found that sulfanilamide promoted phase transformation of a type 5 beta-hemolytic streptococcus, but that it was more active upon the more virulent mucoid type than upon the smooth one. Cooper and Keller (7) found that a strain of *Shigella paradysenteriae Flexner,* which had become sulfonamide-resistant had retained its virulence, whereas a Sonne strain had lost it.

Felsenfeld (8) on the other hand, stated that a strain of *Shigella sonnei* exhibited marked disparity: the colony forms with the greater fermentative activity were the more resistant to sulfonamide drugs as well as to physical agents. Gay and his coworkers (9) demonstrated also that virulence is not affected and that sulfanilamide is not diminished at all by contact *in vitro* with large masses of streptococci.

While a large majority of bacteria can be acclimated to sulfonamides, there are a few strains which show no tolerance whatsoever, and whatever growth is present in the first passage, soon comes to an end or shows no viability in successive passages. Fourneau, Trefouel, Nitti and Bovet (10) found no tolerance to be developed by Aspergillus.

In our experiments a similar case of apparent intolerance to sulfonamides was seen with a strain of *Alkaligenes* which could not be accustomed to grow in presence of sulfonamides. Closely related to such lack of adaptation, it is well to mention again at this point our previous findings described in the experimental portion of this work, that successive passages of susceptible bacteria grown in presence of sulfonamides may finally become nonviable.

Chandler and Janeway (11) found that organisms previously grown in sulfonamide medium are rapidly inhibited when transferred to fresh sulfonamide medium. It has been our frequent experience also that bacteria partially inhibited by a first culture in a sulfonamide medium were inhibited by passage to fresh medium containing the drug.

If one examines the morphologic changes often encountered in our experiments, they clearly show that bacteria, like any other living matter, will undergo changes under the influence of stimuli. Reaction to stimuli is essentially an attribute of life and the fact that bacteria do react in some ways, which for convenience we consider outside of the standards set by us for bacteria, should not cause us to believe that bacteria have changed their vital conditions. Even alterations often observed under the microscope, such as the large size of granularity of the bacterial body, should be interpreted differently as reaction to environment rather than as new characteristics of cells.

Growth of yeast and bacteria has been followed by Knaysi (12) by means of dark-field study. In dark-field work which we are carrying on at this time, the sulfonamide-grown bacteria appear longer than normally, and this may indicate a lack of division along with increase of protoplasmic structure.

Before entering into a discussion of changes in biochemical characteristics, it is important to mention the practicability of using sulfonamide for the isolation of resistant strains. Our experiments were limited to stool cultures and to the use of MacConkey's agar. Neter and Clark (13) tried to apply the use of the drug to selective media for the isolation of paracolon bacilli, but sulfanilamide and sulfathiazole exerted bacteriostatic activity toward both B. Morgani type I and the paracolon bacillus.

We have already said McLeod and Daddi found that a sulfonamide-fast strain of Pneumococcus did not produce peroxide. In this connection, our own findings on eosin methylene blue agar plate indicate that sulfasuxidine inhibits some enzymatic activity of bacteria necessary for the complete oxidation of metabolic products.

It is not clear whether the phosphorylation mechanism is involved in the production of metallic sheen, therefore, it would be interesting to see what reaction would occur among bacteria or fungi that have a different path of glucose oxidation when cultivated in presence of sulfonamides. We have had no opportunity to extend our investigation along this line.

Investigators who have studied the activity of bacterial hydrolytic enzymes in the presence of sulfonamide have reported negative results almost unanimously. Fuller and Colebrook (14) found no sulfonamide intereference with proteolytic enzymes, as peptone and proteins inhibit the action of sulfonamide. Abderhalden (15) found that serum peptidase, pepsin, trypsin, prophylactic proteinases were not influenced by sulfonamides, but that protective proteinases were inhibited at higher concentrations, of the drugs. Fleming (16) in discussing the importance of a small inoculum, found that peptone inhibits sulfonamide action and that such inhibition is dependent upon the concentration of peptone and entirely independent of the concentration of sulfonamides. It seems hardly possible on the basis of reports already cited as well as on our own experiments with carbohydrates, that sulfonamides may change the characteristics of bacterial hydrolases.

There is a view (17) which holds that viruses are organisms which have lost their enzyme systems by a process of evolution and that Rickettsiae represent the missing link between bacteria and viruses.

It would be highly interesting to continue investigations with sulfonamides or antibiotics in order to block the enzyme system and thus possibly to ascertain whether the production of virus-like organisms

Table III

Eosin Methylene Blue—Lactose and Sucrose
Para-aminobenzoic acid 1:1000: 5 cc. added for each 100 cc. of medium.

	WITH SULFASUXIDINE		WITHOUT SULFASUXIDINE	
Bacteria	*No PABA*	*PABA*	*No PABA*	*PABA*
Shig. alkal	+ (colorless)	+ (reddish)	++ (reddish)	++ (reddish)
Alkaligenes 1	—	+++	+++	+++
Shig. sonnei (local)	+++ (colorless)	+++ (colorless)	+++ (black)	+++ (black)
Coli communior 15	+ (reddish)	++ (sheen ++)	+++ (sheen +++)	+++ (sheen +++)
Coli communis 10	+ (colorless)	++ (light wine)	+++ (sheen ++)	+++ (sheen ++)
229 S (Coli)	++ (colorless)	++ (dark)	+++ (sheen +++)	+++ (sheen +++)
Para A	—	+	++	++
Flexner	+	+±	++±	++±
Para B	+	++	++	+++
Shig. dysent.	—	—	—	—
Pseudomonas	+ (no spreading)	+ (some spreading)	++ (spreading)	++ (spreading)
Salm. ab. ovis	+ (wine)	+ (wine)	+++ (sheen +)	+++ (sheen +)
Alkalig. 110	—	+++	+++	+++
Coli communis 10 from—sulfasuxidine plate	+± (wine)	++ (wine)	+++ (sheen +)	+++ (sheen ++)

In parenthesis the appearance of the colonies.

is possible. In our experiments we were able to produce a sulfonamide resistant strain of Proteus, lacking gelatinase, but this was achieved only after many serial transfers.

Para-aminobenzoic acid in many ways still counteracts many of the effects of sulfonamides upon morphological and biochemical characteristics. One explanation, of course, could be that the compound, being a growth factor, will induce normal multiplication and, therefore, normal characters. Bliss and Deitz (18) found that homosulfonamide (Marfanil) is not antagonized by para-aminobenzoic acid and Goetchius and Lawrence (19) noted that none of the N-alkyl-p-aminobenzoic acid derivatives employed shared any effect upon the antibacterial action of sulfathiazole.

Lynch and Lockwood (20) have been able to dissociate the phenomenon of growth-stimulation from sulfonamide-inhibition, and found that substances which are growth-stimulating are not always antagonistic to sulfonamide. Fildes (21) determined that indoleacrylic acid inhibited E. coli grown on ammonium lactate medium only if tryptophane was excluded from the medium. Woods (22) claimed that sulfonamide may inhibit the enzymatic reaction involved in the synthesis of para-aminobenzoic acid.

Changes in pathogenicity have been correlated, wherever possible, with alterations in physiologic and morphologic properties. (23) This, however, does not seem to hold entirely true for sulfonamide-induced changes, perhaps on account of the temporary nature of the influence of sulfonamide.

Scanty literature can be obtained on the influence of sulfonamides upon motility of bacteria. To what is motility due? Is it due to substances covering the bacterial body, which will permit lowering of surface tension? Or should we rather formulate the question as to whether motility has any relation to absorption of food, as it has with many protozoa?

Although it would seem unwise at the present moment to follow the tendency of previous investigators to formulate wide generalizations, the relation between motility and susceptibility to sulfonamides is speculative. The cocci, definitely non-motile, have been inhibited by bacteriostatic agents more promptly than have motile bacilli. This fact appears to have been overlooked by those who attributed the particular sulfonamide susceptibility of the cocci to their gram positivity or to their morphology.

Mention already has been made of the dark-field study now in progress. It is generally assumed that sulfonamide action begins only after a lag-period. However, under the dark-field one observes that a few minutes after mixing the bacterial emulsion with sulfonamides, the type of movement changes and twenty or thirty minutes later clumping of susceptible bacteria begins.

So far the observation has been limited to Proteus vulg. and Esch. coli, in view of the time which must be spent in keeping the slides under observation. In a way it is conceivable that absorption of the drug on the protein surface may bring about a change in molecular electrical charge, and consequent change in movements.

To eliminate the possibility that some of our findings were due to variation in surface tension, we carried out some very simple measurements on the surface tension of media. No significant differences were found between tubes including sulfasuxidine or para-aminobenzoic acid and those containing ordinary media.

Morphological variation in presence of a sulfonamide may depend also on the pH of the medium. Although this doctor has not carried out any systematic investigation of the subject, it was noted in some preliminary work that when the pH of the medium containing sulfasuxidine or sulfathiazole was adjusted below or above that of the control medium, changes like clum formation, flocculation, or granularity were more marked. This, of course, is a somewhat superficial observation, which cannot be corroborated without further work.

Table IV

Eosin Methylene Blue, Difco, containing Lactose and Sucrose.
Glucose (0.5 percent) has been added to the medium.
Sulfasuxidine 1:500 (saturated solution)
PABA 1:1000 5 cc. for each 100 cc. of medium.

	WITH SULFASUXIDINE		WITHOUT SULFASUXIDINE	
Bacteria	*No PABA*	*PABA*	*No PABA*	*PABA*
Coli Communis 10	++ (reddish)	++ (reddish)	+++ (sheen +++) + (1)	+++ (sheen +++) ++ (1)
Bruc. ab.	—	—	++ (1)	++ (1)
Bruc. suis	—	—	+++(sheen+++)	+++(sheen+++)
Flexner 1	+± (reddish)	+± (reddish)	++ (sheen +++) + (dark)	++ (sheen +++) + (dark)
Coli communior 15	+ (reddish)	+ (reddish)	+++ (sheen +++) + (sheen +)	+++ (sheen +++) —
Flexner B	—	—		
Eberth. typhi	+++ (reddish)	+++ (reddish)		
Shig. dysent.	—	—		

(1) after five days.

Table V

Eosin Methylene Blue Agar
Glucose added 1 percent
Sulfasuxidine 1:500 (saturated solution)
PABA 1:1000, 5 cc. for each 100 cc.

	WITH SULFASUXIDINE		WITHOUT SULFASUXIDINE	
Bacteria	*No PABA*	*PABA*	*No PABA*	*PABA*
Aerogenes aerobacter 2	+++	++++	++++	++++
Flexner 1	+ (sheen ±)	++ (sheen +++)	+++ (sheen +++)	+++ (sheen +++)
Bruc. ab. 1	— (2)	+ (1)	+± (1)	+++ (1)
Salm. ab. ovis	+ (sheen +)	++ (sheen ++)	++ (sheen ++)	++ (sheen ++)
Prot. 220 (3)	+ (no spread)	++ (limited spread)	++ (spread)	++ (spread)
Strepto. fecalis	± or—	± or—,	+±	+±
Alkalig. 110	—	++	++	++
Prot. OX19 (3)	± (wine color no spreading)	± (wine color no spreading)	++ (no spread sheen ++)	++ (no spread sheen ++)
Prot. X19	+ (no spreading)	+ (no spreading)	+++ (good spreading—sheen)	+++ (good spreading—sheen)
Flexner from sulfasuxidine (4)	—	—	+ (sheen ++)	—
Flexner from ordinary medium (4)	+	+	+++ (sheen ++)	+++ (sheen ++)
Proteus X19 from sulfasux.	—	—	—	—
Proteus OX19 from sulfasux.	—	—	—	—
Bruc. ab. 2	—	—	+ (1)	+ (1)
Coli communis 10 from sulfas.	—	—	—	—

(1) after three days
(2) delayed growth
(3) American type
(4) grown on the same plate, which has been divided in two halves

Schmelkes, Wyss and Marks, (24) however, noted that an increase of pH induced a more efficient bacteriostasis and stated that the active agent in sulfonamide was the anion. Schmelkes (25) reported that the activity of undissociable sulfonamide molecules increased with the pH, the specific activity of sulfonamide molecules increased with the pH and the specific activity of sulfonamide anions decreased with an increase of pH.

Bell and Roblin (26) claimed that para-aminobenzoic acid is in nonzwitterion form in solution, but that it is a sufficiently strong acid to ionize 99 percent of its carboxyl group in dilute concentration in a medium buffered at pH 7.

According to them, the SO_2 group of any sulfonamide derivative in the ionized form is much more negative than the SO_2 of the same compound in the un-ionized form, presumably indicating that the ionic form of any sulfonamide is more active than the molecular one.

In conclusion, with regard to this particular phase of sulfonamide action, there is no doubt that the drug produces morphologic changes, affects some biochemical characteristics and hinders motility of the bacteria, but these changes do not seem to constitute to any degree a true mutation, nor are they necessarily irreversible.

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LOCAL AND SYSTEMIC REACTION TO AEROSOL STREPTOMYCIN: A CASE REPORT

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Ever since Schatz, Bugie and Waksman (1), in 1944 announced that streptomycin was a potent antibiotic agent, it has become more or less widely used against bacteria against which it has been shown in the laboratory to have a bacteriostatic or bactericidal action. These are chiefly Gram negative organisms.

Some reports of toxicity have appeared from time to time. Hirshfield and Buggs (2) after briefly reviewing a number of reports of reactions, state that a few reactions have been reported and continue to occur but in retrospect many of them may be attributed to impurities in the preparations then available. The same authors (2) give five main types of toxic reactions which are as follows:

1. Irritation and pain at the site of injection. This was more common with the earlier preparations but it still occurs.

2. Histamine—like reactions such as headache, flushing of the skin, fall in blood pressure, nausea and vomiting, may occur immediately after an injection of streptomycin. Arthralagia and fever may occur somewhat later. Like the local reactions, these phenomena were more frequent with the less refined preparations.

3. Sensitization manifestations. Erythematious, urticarial or morbilliform skin rashes and fever may appear after several days of treatment.

4. Casts and albumen may appear in the urine. Usually this is not a serious occurrence for the urine clears when therapy is discontinued.

5. Toxic action on the eighth cranial nerve. During prolonged treatment or even after short treatment with heavy doses, there may develop a subjective sense of vertigo, accompanied by an ataxic gait and reduced labarynthine response to caloric tests. Occasionally a transient deafness may occur but this may be due to the primary disease process and not to streptomycin. No permanent loss of hearing developed in the cases reported by Brown and Hinshaw. (3) Other types of toxic reactions appear in a comprehensive cooperative study by the National Research Council (3, 4-10).

Owing to the fact that the vast majority of cases of reactions occurred when impure streptomycin

was administered, Farrington and his associates (11), undertook an investigation in which a highly purified form of streptomycin said to be at least 95 percent pure, was used. A group of tuberculous subjects was used and were given three Gm. of highly purified streptomycin daily for 120 days. In only two cases was it necessary to interrupt treatment. There was considerably less local irritation than followed administration of the more common form of streptomycin.

The authors, in appraising all the toxic symptoms, conclude that the immediate toxicity of highly purified streptomycin sulfate on long-continued administration is sufficiently low to justify its use in the treatment of serious protracted infections and in most forms of tuberculosis. They add the statement however, that as streptomycin can produce potentially serious toxic reaction, it is inadvisable to use the drug in the treatment of generally benign infections such as recently acquired minimal pulmonary tuberculosis.

The drug was well tolerated when administered intrathecally in doses of 0.1 Gm. Although 0.2 to 0.375 Gm. were well tolerated in some instances they produced untoward reactions of a potentially serious nature in others. Except for the so-called histamine reaction, instances of all of the previously described manifestations were observed after the use of the highly purified material. An intermittent or sustained eosinophilia ranging from 5 to 39 percent appeared in 14 of 16 subjects. Vestibular dysfunction of variable severity appeared uniformly on the twenty-first day. It is not possible to state whether these symptoms are less severe than with the impure product. Deafness occurred in 2 of the 16. In 4 of these cases, the drug was given intrathecally.

Casts and albumen appeared intermittently in most subjects and was uniformly present when the urine was highly acid. Reduction in renal function appeared in only two persons and in one of these, restoration of normal function took place in spite of continuation of the drug.

In two female subjects, *definite evidences of anaphylaxis* developed on the ninth day of therapy. The reactions were similar to those observed after the administration of a number of chemotherapeutic agents; e. g., oxophenarsene hydrochloride, sulfonamides, thiouracil and organic gold preparations.

In both women the sensitivity to streptomycin manifested itself as follows; an itching maculopapular eruption over the trunk and extremities; elevation of temperature; nausea and vomiting; the development of hypotension when administration of the drug was continued and eosinophilia. In one patient, the eruption became purpuric in the area distal to a tourniquet. Bleeding time, clotting time and platelet counts were all normal. When the eruption was fading, purpura no longer appeared distal to the tourniquet. In both subjects, the evidences of sensitivity subsided within a week. During the ensuing weeks, the reaction was repeatedly reproduced in mild form by the intramuscular administration of single small (0.037 Gm.) doses of streptomycin. In one subject, it was possible to resume treatment without reaction five weeks after the original institution of therapy. The other subject still exhibited evidences of sensitivity at the end of the fifth week but was able to tolerate the standard regimen, 12 weeks after the instibition of therapy.

One patient, on the seventy-fourth day of the second course of therapy, developed a moderately acute synovitis of the proximal interphalangeal joints of the hands and feet, accompanied by an eosinophilia of 30 percent. Streptomycin was continued for six weeks after the onset of the synovitis and the synovitis symptoms gradually diminished but were still present three months after their onset.

A Case Report

In view of the reports in the literature relative to streptomycin toxicity, we felt it might be of interest to report the following case history:

E. H., male, 58 years old. Father died at the age of 40 when the patient was five years old and a brother died of pulmonary tuberculosis.

In 1928, when the patient was 39 years old he sustained a slight hemoptysis. The diagnosis of an apical tuberculosis which was made at that time was never substantiated either by clinical symptoms or laboratory findings including sputum examinations.

The patient after a relatively short period of sanatorium care, resumed an active strenuous life with no apparent deliterious effects.

However, in 1937, hemoptysis reappeared and recurred at various times. In 1941, after a severe pulmonary hemorrhage, he was hospitalized for one week and carefully studied. He was discharged from that institution as having no signs or symptoms of clinical pulmonary tuberculosis.

Subsequent to this, the patient continued to cough and expectorate. The sputum though copious, was not foul. The bronchoscopic report was negative except for "chronic bronchial inflammation". Symptoms continued and in 1945, treatment with penicillin aerosol was started. After the fifth day of treatment, patient sustained a severe asthmatic attack and treatment was discontinued and asthma stopped.

In October 1946, the patient had another hemoptysis of a slight degree followed by a pneumonitis with a temperature of 102 degrees F., causing the local doctor to give him penicillin 300,000 units (Romansky Formula), which was (as the patient claimed), almost fatal. He developed an immense swelling of the whole face, which became twice the normal size. After two days, under adrenalin and benadryl, the swelling subsided and he never received penicillin any more from that time on.

In June 1947, he again came under treatment having had a slight hemoptysis in May 1947, and an increase in cough and expectoration with sputum which had become foul smelling.

An x-ray of the chest revealed the old tuberculous process of both apices and an extensive honey-comb bronchiectasis with many small infiltrative lesions of both lungs.

Sputum culture revealed streptococcus hemolyticus and viridans both sensitive to streptomycin and pneumococci resistant to streptomycin.

Especially in view of patient's allergic response to penicillin on intracutaneous skin test by injection of 0.01 cc. (10 mg.) of streptomycin was performed before any streptomycin was started. This reaction was negative. The following day, 0.1 cc. likewise gave a negative reaction.

Patient was started under treatment with streptomycin aerosol on the third day—1.0 cc. every three hours day and night.

Clinically, marked improvement was quickly noted; cough and sputum lessened and there was no more foul odor. General sense of strength and well-being was soon manifest. This continued for eight days during which time, streptomycin aerosol was continuously administered. On the ninth day, he complained of shortness of breath and streptomycin was stopped. That night, he suffered a severe asthmatic attack. All the clinical signs and symptoms of severe bronchial asthma were present on examination.

He responded to the usual measures for control of asthma but suffered from a relapse five hours later which again had to be treated with adrenalin before relief could be obtained.

It was noted at the same time during which the asthmatic attacks were present, that the sites where the intracutaneous streptomycin testings were performed, became red, hot, swollen and tender. Apparently, the reaction occurred in the tissues which had become sensitized by the instillation or application of the streptomycin.

The asthmatic attacks continued but lessened in severity until they stopped occurring after nine days.

The intracutaneous lesions on the arms became less inflammed and smaller and finally could no longer be demonstrated after 20 days.

Comment

A patient who had previously shown sensitivity to penicillin was under treatment for bronchiectasis complicating an old healed tuberculosis. Intracutaneous administration of streptomycin was negative.

Nine days after streptomycin-aerosol treatment was started, the patient sustained a severe attack of bronchial asthma accompanied by a flare-up at the site of the previously given allergy test. This allergy syndrome while more severe than any described by various writers, corresponds in time to those referred to by Farrington and associates; i. e. the symptoms occurred on the ninth day.

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SOME MEDICAL USES OF VITAMIN E*

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Heart Disease

General: Diseases of the heart and blood vessels are the leading causes of death in the United States. They also contribute a major source of disability and economic loss. Research in cardiovascular disease to date has led to a fuller understanding of its pathology and physiology and as a result to more accurate classification of the different types of heart conditions. But, aside from the spectacular surgical treatment of some forms of congenital heart disease, advances in treatment have been all too few, and limited for the most part to managing the symptoms of failure.

In practice the cardiologist's role has been to decide whether or not a given patient actually had heart disease or not, and if so, of what type and of what degree of severity. For treatment he has had chiefly "rest" to offer. The drugs he has had at his

* This material is the second part of a two part article which was first published in the February issue. Complete bibliography follows.

disposal, such as digitalis, quinidine, mercurials, and nitroglycerine have helped to reestablish more normal function, but have left the basic pathology unaltered.

Obviously, therefore, any means of improving the function of damaged hearts by attacking the underlying pathological changes opens up a new era in the treatment of cardiovascular disease.

This is the distinctive value of vitamin E in heart therapy. It reaches the focus of primary damage in most instances and acts directly upon it. Symptoms improve because the underlying pathology is altered, and function then becomes the measure of the degree of actual improvement.

Eleven years ago, one of us (E.V.S.) suspected that the tocopherols might act on angina pectoris and so treated his only male patient, a man who was suffering from this symptom. (38) This led to relief of the pain and a marked increase in his exercise tolerance. Hearing of this case, another of us (W.E.S.) used it on four other cases without beneficial results. Obviously, as we know now, the latter's experiment was doomed to failure because the only form of the tocopherols then available was a crude, cold-pressed wheat germ oil, a product so unpalatable and dilute that no one could take adequate doses of it for long. The first patient was one of the rare exceptions who enjoyed its taste and for whom a small dose was sufficient.

Our interest was revived in the summer of 1945 when a patient of another of us (A.V.), being treated for thrombocytopaenic purpura with vitamin E, demonstrated dramatic improvement in the symptoms of the coincident hypertensive heart disease from which he suffered. (39)

It will be recalled that our use of the tocopherols for thrombocytopaenic purpura had come about due to the animal studies earlier that year of another member of our research team, Floyd R. Skelton (40), and it was he who worked out the high dosage required on the basis of his work on dogs. The next two cardiac cases treated with tocopherols gave equally dramatic results. The first was a patient having hypertensive heart disease with auricular fibrillation and a marked degree of cardiac failure, the second a case of marked cardiac failure following a second attack of coronary thrombosis. These three cases remain as prime examples of the extreme degree of heart disease with failure which can be successfully and rapidly restored to almost normal function with tocopherol therapy.

Since then we have treated about 1500 cases of every type of heart disease, displaying virtually every known complication, and of every degree of severity. From our complete experience the following general conclusions may be drawn:

1. Vitamin E is the most effective known drug in the treatment of heart disease, and certainly the safest.
2. The percentage of cases which show improvement following its administration is high (about 80 percent).
3. The degree of improvement, even in the worst cases, is often marked, and allows a return to activity in many cases of great disability.
4. Improvement continues for months, even years.

We would like to point out that, at least at first, virtually all of our patients had already seen one or more heart specialists and had then turned to us in a last appeal from their prognoses. Now, however, the specialist can no longer be satisfied with diagnosis as the be-all and end-all of his craft, and the philosophic dictum that "many people with heart disease live a long time if they are careful" is no longer adequate therapy.

Much is already known of the mode of action of the tocopherols, as suggested earlier in this paper. Based upon such work and the close daily observation of our patients we have formulated some views of the mode of action of vitamin E in heart disease. We realize that these opinions may need revision later, but at the moment they provide a working basis for the novum organum cordis.

(1) *Capillary Permeability*

As in the case of the thrombocytopaenic purpuras and acute haemorrhagic nephritis the tocopherols may control capillary permeability. As in the latter they probably lessen the internal tissue tension of the inflammatory process and so minimize direct and widespread damage to heart muscle.

As in acute nephritis and thrombophlebitis this control renders the tissues better able to handle the infective factor. Hence any fever may fall rapidly and recovery be rapid. One case may illustrate this.

A boy 15 years old, who had had an attack of acute rheumatic fever in 1941, at that time had spent 25 months in a hospital and had a tonsillectomy. In July, 1946, he had an acute recurrence, with fever of 100.3°, pulse 120, reddened tonsil tags, moderate heart enlargement and both mitral and aortic stenosis and regurgitation. His ankles and one knee showed the usual acute joint reactions. He was promptly given sulpha-merazine and 200 mgm. of Ephynal per day. Three days later his pulse had fallen to 68, his blood pressure to 100/38, he was afebrile, and his joints seemed normal. He was able to walk to the office six days later. In September, 1946, he was able to pull turnips in the field for three weeks on end. He has been well since.

(2) *Capillary Dilatation*

It has been shown (19) that under intensive tocopherol therapy dilatation of old capillaries or even, perhaps, the proliferation of new capillaries may supervene in sclerotic tissues. This can be a major factor in the myocardial improvement that accompanies this new treatment of damaged hearts.

(3) *Oxygen Requirement*

It has been shown on experimental animals that the tocopherols have no effect on the oxygen consumption of normal muscle.

The essential effect of the basic pathological change in many cardiac conditions is a decrease in blood supply either to local or larger areas of the heart muscle. The symptoms of the chronic state of partial local anoxia that ensues are increased by exercise or effort or with such psychological stresses

as excitement or anger. This group includes coronary insufficiency and coronary occlusion chiefly, but what has just been said applies in some degree to the hypertensive heart having some coronary change and to chronic rheumatic hearts showing scarred areas due to inflammatory reaction.

One of the chief storehouses of the tocopherols in the body is the heart. Undoubtedly this is of teleological significance, as we now begin to comprehend it. The tocopherols, by facilitating tissue oxidation, constitute an obvious therapy for the anoxic heart. Two cases will illustrate this.

A man of 45 years of age had had attacks of coronary thrombosis in July, August and September of 1945. When first seen in June, 1946, his blood pressure was 140/100, his pulse 100; there was minimal leg oedema, and he could walk only one half block before being stopped by pain. Within three days of starting treatment with Ephynal he showed improvement, and this has been continuous since.

Within two weeks time, for example, he could walk four blocks in 11 minutes without pain, and his blood pressure was 120/80. Within one month he could swim two lengths of a pool. Since that time his activity has been about normal. He leads an exciting life as manager of a professional wrestler and a sports promoter. On January 6, 1947, he went skiing in the Laurentians, and performed on the famous Hill 80, at St. Adele, Quebec!

A man of 57 years had an acute coronary accident in 1934, necessitating morphine for a week. His convalescence required eight months, half of that time being spent in bed. Then he returned to selling motor cars—very carefully. In 1937 another coronary attack totally incapacitated him. In September, 1945, he experienced a third coronary which was followed by marked electrocardiographic changes.

When seen by us for the first time, in July, 1946, he would not venture out of his chair to walk six feet to his tobacco. He could play bridge with unexciting friends, could scarcely talk for dyspnoea and anginal pain. A complicating bronchial asthma was present. His blood pressure was 142/90. After the first week of tocopherol therapy he had no more angina.

In August, 1946, he fished all day, spent two hours cleaning his fish, and played hectic bridge until midnight. Two days later he played nine holes of golf. Up till January, 1946, he had had 12 abnormal electrocardiograms. Now his tracing would be called "suspicious" of coronary change.

(4) *Effect of Thrombosis*

Improvement in our cases of coronary occlusion is almost invariably rapid and the patient in the majority of instances is soon able to return to normal activity. Further attacks of occlusion very rarely occur in those patients who have been under treatment for more than two weeks. There have been very few exceptions to this rule. This is of enormous importance in the prognosis of cases of coronary thrombosis. Moreover, this new safety factor in treatment with the tocopherols increases with time.

Those already familiar with this safety factor are so convinced of it that one of our Boston friends (40) now lets his acute coronary thrombosis cases get up in three to four weeks and has so far noted no ill effects. We have been afraid to do so, but the rationale is probably not incorrect.

By directly attacking the thrombosis, by decreasing capillary permeability and increasing local capillary dilation, as well as by decreasing the oxygen requirement of the staggering heart muscle, the tocopherols offer their maximum assistance to the recent case of coronary thrombosis.

It is conceivable that they decrease the extent of the infarct itself and after a tiny thrombosis may even prevent infarction. By local capillary dilatation they improve oxygenation in the muscle at the edge of the infarct, and by decreasing the myocardial ischaemia, help the embarrassed heart to continue function. Consequently in these cases we begin tocopherol therapy at once, and, where possible, by intramuscular injection. Again, to quote our friend Dr. Mills, "the electrocardiogram returns to normal in less time and in more cases than formerly."

When one sees the speed with which a fresh thrombosis in the leg responds to tocopherol therapy, he can easily realize the importance of beginning therapy of a coronary thrombosis at the earliest possible moment. Although the early case is the ideal one, of course, the tocopherols are strikingly effective in older cases too.

We can cite one patient who had an attack of coronary thrombosis seven years ago, and who had 15 electrocardiograms since, all showing the characteristic pattern of coronary infarction. During all this time his exercise tolerance had been extremely low. He could merely go down to his hat shop for 15 minutes' work twice a week. After tocopherol treatment of three months' duration this patient's electrocardiogram is now completely normal. During the Christmas rush of 1946, he not only supervised his business, but worked as a clerk for nine hours daily.

Scar Tissue

Many pathological hearts show replacement of muscle with scar tissue in either small or large areas. Now Steinberg was able to demonstrate resolution of the lesions of Dupuytran's contracture in some cases; an effect scarcely obtainable without some degree of dissolution or softening of scar tissue. In spite of the negative animal experiments of Mason, is it not conceivable that scarred human hearts may be less scarred after prolonged tocopherol therapy?

Moreover, by the use of an amplifying Electronic stethoscope, Dowd (42) has demonstrated changes in the sonority and quality of valvular murmurs under tocopherol treatment. It is not impossible, as bold as the conception may sound, that the tocopherols may even soften scarred valve rings—or perhaps the tension on those rings changes as heart volume changes. We have at least fluoroscopic evidence to suggest that many enlarged hearts shrink under treatment.

To summarize, our theory of the mode of action of the tocopherols in heart disease is that they:

1. Decease capillary permeability.
2. Produce capillary dilatation.
3. Decrease the anoxia of the cardiac muscle.
4. Prevent further thrombosis and help to resolve existing thrombi.
5. Invade scar tissue with fresh blood vessels, thus softening or relaxing it.

This theory—and we should stress that it is merely our working hypotheses—explains all our cardiac results, and until a better one is propounded may stimulate the extension of tocopherol therapy to many pathological conditions other than those we have specifically mentioned.

Dosage

The size of the dose is the most important factor in this treatment. For practical purposes, at least in cardiology, alpha tocopherol is the effective fraction of vitamin E. The other tocopherols are either less active or inactive. The current practice of labelling concentrates of wheat germ or corn oil as "mixed natural tocopherols" is misleading and should be discontinued. Either emphasis should be put on the alpha content only, or the total tocopherol values should be expressed in their equivalent of alpha.

Doses are huge in the light of previous vitamin E therapy. Ours is not replacement therapy, obviously, but a new use of medicinal agent already well known. The drug houses have themselves to blame, perhaps, for the poor repute in which tocopherol therapy has been held by so many practitioners.

They are still manufacturing and selling vitamin E in three minim capsules and 3 mgm. pills, these being almost useless, of course. Prices are set at levels that make prolonged medication difficult for the poor. One wonders what the state of the treatment of diabetes mellitus would be today if all cases were treated with only one or two units of insulin per day, and if governmental agencies made no effort to mitigate the cost of therapy.

200 mgms. of alpha tocopherol appears to be the average dose, whether for control or maintenance, in 80 percent of cardiac cases. (43) The rest demand more at first, up to 600 to 900 mgms.

Doses as large as 5,000 mgms. have been given to normal humans without danger. (9) However, in heart disease one of us (W. E. S.) feels that there are two types of cases in which harm may be done by initial large doses of tocopherols; treatment must be instituted cautiously and slowly in these conditions.

The first of these is in chronic rheumatic heart disease with incipient failure. Too much of the tocopherols given too rapidly will, in perhaps one-third of the cases, throw the halves of the heart into worse relative balance and precipitate more severe failure. In these patients we give 100 mgms. daily for two weeks, then 150 mgms. for one or two weeks, and only then give them their optimum dose of 200 to 300 mgms.

The second category is the patient where a marked degree of hypertension already exists. The tocopherols improve the tone of heart muscle and so may actually raise the elevated blood pressure above a safe level. While we have not yet had a disaster from this cause, we shun even the appearance of evil and start such patients out on small doses. In essential hypertension the tocopherols appear to be useless, but in hypertensive heart disease tocopherol therapy improves cardiac function in the same way and to the same degree as in any other type of damaged heart. The blood pressure in such patients falls to normal in approximately one-third of the cases, falls to a significant degree in another third, and is unchanged in the remainder.

A man, age 62 years, had suffered for at least three years from hypertensive heart disease, accompanied by angina, paroxysmal nocturnal dysponea, moderate enlargement of the heart, auricular fibrillation. His blood pressure was 200/112. Anginal pain prevented him from working. He was given 600 mgm. of tocopherols. In four months time his blood pressure had fallen gradually to 160/80, with regular sinus rhythm. On June 11, the hottest day in Toronto in 1946, he put in a full day's work, then walked 1½ miles without experiencing any distress. Since October his blood pressure has been 130/80. His wife died a lingering death of cancer without producing any recurrence of his symptoms.

Another of us (A. V.) begins treatment of his patients with a daily dose of 300 mgm. of alpha tocopherol or its equivalent, given in divided doses with each meal. This dosage is maintained for 10 to 14 days until satisfactory clinical improvement is noted. If none develops the dosage is raised still higher. In any case, once one has reached the greatest improvement that can be achieved and this has been maintained for several weeks, the dosage is gradually reduced to the minimum that will keep the patient as well as he has been on the larger dose. This maintenance dose is rarely less than 200 mgm. of alpha tocopherol, and will be higher in late winter than in summer, as is mentioned below.

A favorable response to tocopherol therapy may begin at once, but oftener does not appear for five to 10 days. Some of our best therapeutic results have been obtained in people who had no help for as long as the first six weeks of treatment.

Further improvement may still be found to occur after a year or more of tocopherol therapy. Moreover, for every patient there is an optimum dose, somewhere in the neighborhood of 200 mgm. A smaller dose gives little or *no* results; a larger dose is not necessary. In the acute cardiovascular case, whether it be acute coronary thrombosis or acute apoplexy, the appropriate means of giving the tocopherols is by intramuscular injection, obviously, for this decreases the interval required to obtain control of the patient to a third or half the usual time needed.

As has been shown elsewhere (43), the dose of thyroid varies with the season, being least in summer and greater in winter, and this is also the case with the tocopherols, another type of anti-oestrogen. The diet of summer contains some vitamin E, the

diet of winter much less. Such a variation in tocopherol dosage could have been anticipated.

Other Therapeutic Agents

Iron is contraindicated. It seems to "bleach out" the tocopherols. (44) Anaemias of long standing associated with cardiac disease may disappear under the tissue oxygenation of tocopherol therapy.

Digitalis, aminophylline, nitroglycerine, or mercurials may be used in conjunction with the tocopherols wherever indicated. Only a maintenance dose of digitalis need be given to those already on digitalis therapy until the effect of tocopherol replacement has become apparent. On the other hand, a patient who has already had a large amount of tocopherols is often remarkably easy to digitalize, perhaps on three grains of digitalis folia, and the danger of digitalis intoxication at an early and low level of digitalis dosage must, therefore, be kept in mind. One must be careful, too, that the diuresis produced by the tocopherols in so many heart patients in failure does not induce signs of digitalis intoxication due to mobilization and concentration of the digitalis in tissue fluids.

Hospitalization

In these days of severe overcrowding of hospital facilities, of inadequate staff, of harried doctors and nurses, our experiences with tocopherol therapy for damaged hearts have been especially gratifying. Responses are usually so good and so rapid, and the treatment is so safe, that hospital care is rarely necessary.

Many a patient has been taken from his sick bed and made ambulatory. Frequently he has been returned to full time work. This is in marked contrast to the history of the average severe cardiac who barely walks about in the interim between periods of bed rest. Some of our best known cardiologists have made a reputation on "6 weeks in bed" and little treatment beside!

Prophylaxis

The most important implications of this work, of course, are that proper dietary revision may prevent or at least delay the appearance of cardiac disease in a large proportion of the population who now become its gasping victims. Sir Maurice Cassidy, the King's Physician, in the *Lancet*, October 26, 1946, reviewed the startling increase in cardiac disease over the last 50 years.

He stated, and we have had this observation confirmed by older physicians of our acquaintance, that angina pectoris and coronary thrombosis were rare at the beginning of the century. Cassidy reviewed the classical explanations advanced to explain this comparatively recent increase, including greater stress of living and the modern increase in life expectancy, and showed that none of them applied to this phenomenon.

It is possible that this increase is explained by the removal from the general diet of some of its essential germinal vitamins in the process of making attractive white flour free of racidity. This wasted germ is now the source of much of our tocopherols and in our hands is trying desperately to repair the ravages of the miller's greatest triumph. We should speedily return the wheat germ to flour. England has already begun to do so.

Neurocirculatory Asthenia

We now have several patients giving a history of heart disability, but displaying no objective evidence of this beyond some increase in heart rate. These people had been previously diagnosed as neurotics, examples of functional disorder of the heart, or pure malingerers. They responded fully and completely to tocopherol therapy, as was to be expected, and it is most gratifying to see them now able to return to full activity and throw off the stigma of their former diagnoses. In these patients we hope that the maintenance dose may prove to be less than the therapeutic dose.

Mr. A. L., age 38. He has always been of a nervous disposition, complaining of weakness as well as palpitation and rapidity of the heart. He tried to join the army but, after exhaustive tests involving examination under conditions of rest and sedation, he was turned down on the diagnosis of neurocirculatory asthenia. This man has been restored to normal on tocopherol therapy, with a decrease of heart rate to normal, and the disappearance of all symptoms.

He stopped treatment for 10 days and once again became nervous, excitable and weak, with a rapid pounding heart. When he returned to tocopherol management he remained well and active.

Changes In The Electrocardiogram

1. *Effect on Cardiac Irregularities*
   A. Auricular Fibrillation
   B. Premature Ventricular Systoles

These two types of irregularities in rhythm are those we have encountered most often. With auricular fibrillation we have noted only 15 to 25 percent who have been returned to normal sinus rhythm. One of our successes was in a patient who had fibrillated for 12 years. Improvement can be accounted for, where it occurs, by an increase in auricular tone and is more or less independent of any increase obtained in exercise tolerance.

There appears to be a definite effect on premature ventricular systoles, both in those cases in which the extra systoles come in "showers" and in those cases where one finds "coupling". Practically all patients with this irregularity are either completely relieved or else reveal only an occasional premature ventricular systole.

2. *PR Interval*

The PR interval which is prolonged above 0.2 seconds is most commonly caused by one or two factors—(a) auricular dilatation secondary to mitral stenosis and/or regurgitation (b) digitalis intoxication. In the first group of cases the PR interval has been found almost invariably to become shortened on tocopherol therapy.

In the second group, where the PR interval is prolonged due to digitalis intoxication, the tocopherols may exaggerate the toxic condition because

of the patient's increased sensitivity to digitalis on tocopherol therapy. Therefore, these cases should not be given digitalis until all signs of digitalis intoxication have disappeared. They may then be given only small maintenance doses of digitalis.

3. *Initial Ventricular Complex*

In a period of observation extending well over a year no changes in aberrant QRS complexes have been noted. For example, the most common of these (bundle branch block, Wolff-Parkinson-White syndrome, and slurring and notching) have shown no change.

4. *Final Ventricular Complex*

If the ST segment is displaced as a result of digitalis intoxication one must turn to the same procedure as mentioned above in the discussion of the toxic PR interval. The remaining types of ST displacement, whether caused by "ventricular strain" or by coronary artery disease, will revert toward normal under tocopherol therapy.

T waves which are isoelectric, diphasic, or inverted because of organic myocardial disease become less inverted and, in time, tend to become erect. This does not seem to apply to the "postural" inverted T_3 or to the inverted T_3 found in some normal people.

5. *Slow Changes*

As has been said, tocopherol therapy leads to continued improvement over the course of months in most patients. There is very rarely any immediate or early change in the electrocardiogram such as occurs with digitalis, atropine, quinidine, and epinephrine, for tocopherol has no toxic effects on the heart. Where marked changes appear in the tracing the amount of myocardial scarring may be considerable. Heretofore this has been regarded as permanent.

Now it is noticed that after three to six months have elapsed, there may be a good deal of improvement in certain abnormal electrocardiograms. These favorable changes, of course, are commoner and more marked in patients treated from the onset of their disease with tocopherols, as in an acute coronary thrombosis, for example. This slow change in the electrocardiogram is further evidence that the action of tocopherols is on the basic pathological process.

Radiographic Changes

Those hearts which cast markedly enlarged radiographic shadows, particularly involving the left ventricle, show the greatest decrease in the size of the shadow. This is caused, perhaps, by an increase in ventricular muscular tone and so affects the dilatation factor but probably does not affect the hypertrophy factor. The six cases with effusion we have studied have cleared up all signs of the effusion within five days. We have not used the tocopherols in any cases of acute suppurative pericarditis.

Catalyst

In the beginning there may be a serious therapeutic shortage of the tocopherols. As soon as this treatment attains the recognition it deserves, it will be difficult to secure what is needed to maintain high dosage treatment. The chemists must find us either a good synergist for or more effective preparations of vitamin E.

In the case of muscle dystrophy inositol enhances the activity of alpha tocopherol by thousands of times (45), and later studies indicate that there are several sugars that are even more effective synergists. Cytochrome C may prove to be an effective adjuvent, vitamin C seems not to be one. (6) Vitamins B and E occur together in cereal germs. It could be anticipated that deficiency syndromes associated with the one should concomitantly reveal signs and symptoms of defect of the other. There is evidence that such is the case. (46) And one has only to read such a review of vitamin B therapy as Biskind's (47) to realize how these two vitamins interlock and probably overlap. We are at present investigating a possible inorganic synergist, just as calcium and phosphorus are synergistic to vitamin D.

Not A Panacea

There is a real danger of giving the impression that the tocopherols are a cure-all. It should be remembered that in our limited experience fully 15 percent or more of cardiac cases treated have not been helped demonstrably, and we, of course, have had patients die—as all patients, and all cardiac cases especially, have a way of doing. But this new mode of treatment should, one suspects, wield the sword of Horatius in the van of those who fight the "Men of Death".

For too long we have thought of vitamins as food accessories or catalysts, and, therefore, as being needed in only small supplements in our diet. But surely it is now obvious that the vitamins should be regarded as chemotherapeutic agents, their specific peculiarity being the fact that they exist as traces even in our sophisticated foods. Nature devised them for prophylaxis long before we thought of them for cure.

Summary

1. A consideration of the laboratory history and the chemico-physiological relationships of the tocopherols indicates that they should play a much wider and more significant role in the body than the "bit part" of a fertility vitamin.

2. The general rule is advanced that wherever improved oxygen utilization in tissue or better capillary circulation is a desideratum, the tocopherols may be of value.

3. Certain conditions such as indolent ulcer, thrombophlebitis and phlebothrombosis, thrombangiitis obliterans and related vascular conditions, mazoplasia, myositis, fibrositis, cerebral thrombosis, nephritis, purpura and, most importantly, heart disease are discussed in detail. In all of these, the tocopherols may be helpful.

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No summary of our studies can ignore the vital part Mr. Floyd Skelton has contributed to them from first to last. We hope to accord it more suitable acknowledgement later.

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PERSONAL EXPERIENCES WITH CARCINOMA OF THE RIGHT HALF OF THE COLON IN PRIVATE PRACTICE

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In a total personal series of 214 cases of carcinoma of the large intestine in private practice, there were 22 cases of carcinoma in the right half of the colon. The localization of the tumors is as follows:

ileocecal	4 cases	1.8 percent
ascending colon	6 cases	2.8 percent
hepatic flexure	6 cases	2.8 percent
transverse colon	6 cases	2.8 percent

There were three cases in which there were multiple localizations: One patient had the original tumor in the sigmoid; then localizations developed at later periods up to two years in the ileocecal region and in the rectum. The patient recovered 22 years after the last operation.

The second patient exhibited the primary position of the malignancy in the rectum and the second localization, 10 years after the first, was in the hepatic

flexure. This patient became well one year after the second resection. The third patient had a carcinoma of the cervix treated by radiation; eight years later a carcinoma developed in the hepatic flexure. The patient was well two years after the last intestinal resection—operation.

General Considerations

In none of the cases in this group was there any hereditary factor. There was no history of any form of trauma upon which the later appearance of any malignancy could be predicated. This corresponds with the opinions of Teutschlander (3) and of Ewing (1, 2), that no cancer follows trauma in a healthy region. Teutschlander (3) believes that trauma may activate an already existing lesion; but, according to Ewing (1, 2) the grounds for this supposition are unsatisfactory, and he rejects the idea that trauma may endow neoplastic cells with greater powers of growth.

In the cases with single tumor localizations, there was no indication of the presence of any polypi upon which the malignancy could have become engrafted. In the rectum to hepatic flexure case, however, this possibility was distinctly present.

At the second operation for the removal of the hepatic flexure, the entire ascending colon was also removed. The specimen contained several isolated small polypi in the cecal pouch and a little above this area. On histological examination the major tumor was an adenocarcinoma. Each of the polypi contained numerous mitotic figures, but no indication of an out-and-out malignancy. The implication is quite obvious.

Lymphatic Spread: Local extension of the malignancy into the regional lymph nodes was present to a remarkably small extent. Nevertheless, there is frequent reference in the laboratory histological reports to penetration of the tumor through the peritoneal coat of the bowel and to its spread into neighboring fat and connective tissue.

In the cervix to hepatic flexure case, it was established during the second operation that the swelling in the bowel lumen was continuous with a large induration behind it extending into the retroperitoneal space. It was assumed that this was also of a malignant nature, but the resection was done none the less, even though it could not be considered a "radical" one. Nevertheless, the patient is well two years later and no mass can be palpated in the abdomen or elsewhere and an x-ray of the bowel is negative.

In practice, the most favorable results are to be expected where the tumor is entirely within the bowel lumen. Somewhat less favorable prognoses must be made where the tumor has penetrated the bowel wall but has not spread any further as shown by the absence of any adhesion to neighboring structures. The least favorable cases are those where such spread has occurred; as a matter of fact, most of the recurrences occur in this group. From the standpoint of local recurrence and distant metastases, the extent of the growth along the long axis of the bowel is less important than the growth and spread of the tumor through the thickness of the bowel wall with extension outside. Local preoperative complications.

There were comparatively few local complicating factors in this group of cases. These included (1) diverticulitis, (2) perforation or penetration with or without extramural abscess, and (3) obstruction. It is difficult to establish the causal relation of any diverticulum to the malignancy, because both may be present in a given area without any such relation and, in the cases, with perforation or penetration, the diverticular structure would be unrecognizably destroyed. In the presence of a localized abscess, it is necessary to first drain the abscess before any radical resection can be attempted.

One middle aged woman developed right upper quadrant symptoms and the roentgenogram showed a lateral defect in the hepatic flexure which looked like an extracolonic lesion indenting the bowel wall. On exploration an extramural abscess was found, incised and drained. The defect persisted radiographically, however, and at a second operation a carcinoma was demonstrated which was radically resected in one stage. The patient is well 2½ years later.

Biopsies: Biopsies are only possible in the last group of cases. Whenever a malignancy is suspected a piece of tissue from the wall of the abscess, or from the area of perforation can be removed when the abscess is drained for this purpose. Otherwise preliminary biopsies are not possible.

Preparation of the patient for operation.

1. Preoperatively present complications and/or intercurrent disease.

Cancerous disease, as illustrated by this group of cases, and as is well known, occurs in the later periods of life and the individuals are commonly afflicted with associated and/or complicating conditions and abnormalities which are important factors in the final results.

Such conditions include hypertension, renal disease, cardiovascular disease in general and coronary artery disease in particular, and their associated thrombo-embolic lesions such as pulmonary and cerebral embolism and/or hemorrhage. In all of these cases, judgment of the risk is important. The latter is based upon the length of time the disease has existed, the number of repetitions of acute episodes, the amount of demonstrable damage which is present, the amount of compensatory effort and of reserve which is still present and available, and the frequency of occurrence and the number and extent of their complicating effects upon other organs and systems.

In integrating all of these facts, laboratory investigations are not decisive and, for this reason, personal experience is a most valuable guide. The patient should, therefore, never be without the attention, and the surgeon should never be without the help and advice of a competent internist and/or cardiologist. Cases with renal disease should be well studied from this standpoint also and the risk contributed by this factor should also be evaluated.

These complications and associated conditions

(cardiovascular, renal disease, etc.,) are improved as far as lies in ones power with medical measures. Frequently time and rest in bed is a most important factor as well as the ability to judge the proper moment for operation. It is regrettable that corrective measures for these conditions are limited.

2. General Factors.

The important general factors to correct include (1) malnutrition and dehydration, (2) any protein deficiency and hypoproteinemia, and (3) any anemia. Correction of these items, fortunately, always go together. The measures for this include parenteral glucose in saline, hydrolysates, and plasma and blood transfusion. These are given according to indication and to the extent necessary for correction of the deficiency. A sufficient quantity of the necessary vitamins are also supplied.

The usually accepted maintenance dose for protein replacement is 1 gm. per kilo of body weight. Varco (4) has suggested the following regimen based on percentage body weights.

1. When the percentage of body weight loss is at least 5 to 10 percent, three to five days of proper feeding is sufficient.
2. When the percentage of body weight loss approaches 20 percent, ten to twelve days of proper feeding are necessary.
3. When the percentage of body weight loss approximates 25 to 30 percent, nearly three weeks of adequate feeding are required.
4. When the percentage of weight loss is in excess of 35 percent, at least one month of thorough feeding is required.

In the preoperative preparation, and in the postoperative management of operative cases of this calibre, this dosage does not take into account the length of time for which this protein deficiency has existed. In my experience, in long standing deficiency states, these dosages must be increased and kept up, perhaps, for longer periods.

3. Diabetes.

Diabetes is also a fairly frequent complication. Fortunately with modern methods, this factor presents no difficult problem.

If good recovery from any operation, and efficient healing of the operative wounds are to be expected, all of these complications and deficiencies must be corrected and made good, before, during and after operation. Success depends many times upon well carried out, efficient and unhurried preparation of the patient to the extent commensurate with the amount of deterioration and the degree of any complication, as well as on a well planned and well carried out operation. Emphasis must be placed upon the fact that the operation must never be hurried.

4. Local Bowel Preparation.

Local preparation of the bowel is done as thoroughly as possible. Nevertheless, if drastic cathartics are necessary, a sufficient interval should be allowed to enable the bowel to recover from the extraordinary stimulation before operation, as otherwise there is much discomfort from postoperative distension.

Anesthesia: Spinal anesthesia was used exclusively in this group of cases except when contraindications were present. However, the usually accepted contraindications—cardiac disease, advanced pulmonary disease, hypertension, etc., were not so considered, as it is my experience that even under these conditions spinal anesthesia is the best form of anesthesia and carries no increase in the risk.

One contraindication was considered absolute, namely the presence of an intestinal fistula with or without fecal discharge, or a discharging sinus leading to an abscess cavity, either one in the immediate proximity of the proposed point of entry of the spinal needle. When spinal anesthesia was impossible, inhalation anesthesia was used. Rectal anesthesia was never considered.

Surgical Considerations

Operability: Five of the cases in this series were not clinically suitable for radical operations. Two cases were admitted in moribund condition. Three cases were found to be in too advanced condition for any radical procedure at the operative exploration. The total operability of the cases in this group was 55 percent.

Operative Treatment

Non-Obstructive Resections: In general the technique of the resection has followed the usually approved lines. Frequently there were modifications in accordance with the local physical conditions. They were most commonly necessary because of the presence of (a) extensive adhesions about the site of the tumor with or without adhesion to, and possibly invasion into a neighboring loop of bowel.

On one occasion—previously referred to—the sigmoid was adherent to the ascending colon and cecum and the primary cecal tumor had grown into the sigmoid. Both resections were done at the same time. On some occasions (b) there were chronic penetrations without abscess formation which permitted, nevertheless, radical resections in one stage without colostomy. (c) In some instances there was more than the usual local glandular involvement and, in order to conserve the necessary blood supply without interfering with the radicality of the operation, the technique of the removal was somewhat modified.

Tumors in the right half of the colon are the least difficult. Tumors in the cecum, in the ascending colon, in the hepatic flexure, and in the transverse colon up to a short distance from the splenic flexure were treated by removal of the cecum, the ascending colon, and of the transverse colon to and beyond the site of the tumor, with closure of the stump of the terminal ileum and of the stump of the colon, and side-to-side ileotransverse colostomy with the stump of the transverse colon. If, on completion of the removal of the tumor-bearing area, there is not sufficient room for the anastomosis between the ileum and the stump of the transverse colon, the anastomosis could easily be made with the sigmoid—ileosigmoidostomy.

Although he has not yet done so, and because this

method has worked so well, he proposes to follow it in resections of the splenic flexure also when the opportunity next presents itself. Restoration of the intestinal continuity would then be done by an ileosigmoidostomy.

Multiple Stage Operations: Except in the presence of bowel obstruction, or of an extramural abscess necessitating preliminary drainage, no case in this group was done in multiple stages. The reasons for this are twofold: the right side of the colon and the proximal transverse colon lend themselves especially well to one stage resections; and, in any case, it is my experience that multiple stage operations carry a more extensive morbidity and a greater eventual mortality than one stage operations because of the technical difficulties and the greater danger of infection.

Obstructive Resections: In the presence of any degree of obstruction, the bowel was first thoroughly decompressed by a preliminary ileostomy or cecostomy. The actual removal of the tumor-bearing area was done at a second stage. Usually the latter was not particularly more difficult than in a primary resection, but there is no doubt that the danger of infection is greater.

Colostomy: It was not necessary to do an ileostomy or cecostomy in any case in this group as a palliative measure.

Chemotherapy: Ever since chemotherapy has been available for clinical use, it was used in the cases in this group as a prophylactic measure against infection. Preoperatively all cases were given sulfasuxidine by mouth for at least three days prior to operation; at the close of the operation, sulfanilamide powder was insufflated all over the operative field in a very thin layer; after operation, penicillin and sodium sulfadiazine was given in frequent intervals and in sufficient dosage.

Postoperative Management: The routine immediately after operation included: (1) Parenteral alimentation with glucose in saline either alone or combined with intravenous animoids, and with plasma and/or blood transfusions, all given in conformity with the severity of the indication; (2) as soon as possible this was displaced with mouth alimentation to the capacity of the individual and with adjustment of the parenteral supply, solid food being withheld until the bowel function is restored; (3) necessary care of any preoperatively present general medical complication and/or associated condition.

Early Ambulation: In this series no patient was permitted out of bed until the general condition, the state of the local healing in the intraabdominal wound and in the abdominal wall was satisfactory. In my experience early ambulation in this type of case is neither consistent with the strenuousness of the operation, and the strength of these individuals, nor does it eliminate those complications which early ambulation is said to prevent. In this series there was no instance of postoperative thrombosis and/or embolism.

Radiotherapy: No case in this series received preoperative radiation as a prophylactic measure. Postoperative radiation was, however, given but as time has gone on, the intensity of this has been diminished because of several experiences this author has had, due to late effects of the radiation.

Postoperative Complications: There have been no complications in this group of cases after operation.

Results

A summary of the results in this group of cases is as follows:

The cecum.

There were a total of four cases in the cecal region. The facts are:

exploratory *			1 case
radical resections			3 cases
operative death **	1 case		
follow-up "well"	9 years	1 case	
	over 5 years	1 case	

* The patient was admitted with the clinical picture of an acute appendicitis. At operation, there was found in addition a diffuse abdominal carcinosis from a primary lesion in the ileocecal region.

** The large tumor was adherent to the gall bladder and the latter was, therefore, necessarily removed in addition to the resection.

** The term "operative death" employed hereinafter indicates that no definitive objective cause, such as peritonitis, hemorrhage, etc., was demonstrable.

The ascending colon.

There were six cases in the ascending colon of which the details are as follows:

inoperable			1 case
radical resections			5 cases
operative death*	1 case		
9 years	1 case **		
5 years	1 case ***		
3 years	1 case ***		
no follow-up	1 case		

* This case occurred in the early days of the local use of sulfanilamide powder. At the conclusion of the operation the powder was insufflated into the retroperitoneal space and in the general operative field. It is this author's opinion that much of the powder was used because the latter caked in the retroperitoneal space and led to an abscess which spread behind the mesenteric root.

** The patient had gone nine years without any signs of illness. He had originally received a great deal of postoperative radiotherapy. Then he developed an acute intestinal obstruction from which he died, which was due to a shrivelling of the mesentery and small intestines which is considered by this doctor as a late radiation effect. (5) Compare with section dealing with radiation therapy.

*** Both of these patients died of tumor recurrence.
The five year case was first explored by another surgeon who, thinking the tumor inoperable, did a palliative side-tracking colocolostomy. One year later a radical resection was performed. The patient then went five years before he developed metastases in the liver.

Although this is an extensive resection, the patients who have followed this plan have done well and, this doctor has had no cause for regret. This has enabled him to avoid the postoperative messiness and the danger of a secondary closure when other methods of resection were done, especially vorlagerung operations.

The Hepatic Flexure: There were six cases in the hepatic flexure, the details of which are:

operation refused (inoperable)		2 cases
admitted "moribund"		1 case
explorations		2 cases
preoperative peritonitis	1 case	
inoperative—ileostomy	1 case	
resection—"well" over 5 years		1 case

The transverse colon.

There were six cases in the transverse colon of which the details are:

operation refused (inoperable)		2 cases
"moribund" on admission		1 case
acute intestinal obstruction		
exploratory		2 cases
liver metastases	1 case	
locally inoperable	1 case	
resection—no follow-up		1 case

Summary

In a total series of 214 cases of carcinoma of the large intestine, 22 cases occurred in the right half of the colon. These were studied in regard to statistical information, preparation of the patient, various forms of operative treatment, chemotherapy, radiation therapy, and results with follow-up observations.

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PSYCHONEUROSES IN RELATION TO GENERAL MEDICINE

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In understanding the relationship between psychoneurotic manifestations and clinical medicine in all of its ramifications, one must first endeavor to form a clear conception of the underlying factors capable of producing functional disturbances in the domain of the nervous system.

Not infrequently does it happen in the development of an individual, that for the slightest reason, all subjective disturbances referable to the ear, nasopharynx or larynx, are primarily brought to the attention of the otolaryngologist. Should the subjective disturbances have an apparent relationship to the function of the ovaries; vesical and biliary organs or of other abdominal viscera; respiratory and cardiac organs; or to the function of the eyes, then all such cases are referred to the respective medical or surgical worker.

Such an attitude on the part of the lay-patient is psychologically logical and correct. But from a medical standpoint, the above attitude frequently leads to serious errors. Therefore, there are disturbances which have no fundamentally serious relationship to any given abdominal or thoracic viscera, but belong to purely mental functions which dissociate the work of the various elements which enter in formation of harmonious display of organs and tissues.

What precisely characterizes the individual in all such cases is not the multiplicity of symptoms, not the innumerable functional disorders which may simulate organic diseases, not the painful sensation which he or she experiences, but only a special state of mind—a special mentality.

Human machinery is so complex in its various operations that everyone of us, otherwise sound, experiences now and then some indication of a functional disorder; either there is a gastric manifestation; vague pain; cardiac palpitation, or a fugacious neuralgic discomfort. But being normally constituted we give all such symptoms their proper interpretation and our attention is not firmly arrested on them. Thus we continue our activities.

Furthermore we are able to overcome unpleasant circumstances which may arise at any time. We may even surmount obstacles of a most serious nature. Our relative indifference to all such conditions constitutes a normal state of mental health.

On the other hand, the individuals whose attention is held firmly and for a prolonged period of time by those subjective disturbances enumerated above present a type apart, an abnormal type of humanity and therefore require special consideration. These personalities view the least unpleasant event as a catastrophe, and develop obsessive ideas and hold on to them for months and years. Their association of ideas illustrates that fears, anxiety and abnormal inhibitive or abulic phenomena make their appearance with the greatest facility and

apropos of insignificant occurrences. Suggestibility and auto-suggestibility are exaggerated and their reactions to external or internal stimuli are intense.

Fuller elaboration of such individuals is now indicated for a clearer understanding of the subject under discussion. First of all, psychoneuroses should be firmly distinguished from mental deficiency. The latter is usually congenital and inherent and is the direct result of a morphological or physiological abnormality of the nervous structure. Of course psychoneurotic manifestations may appear in mentally defective individuals, but there is no unusual relationship between the two, and we are considering here only intellectually normal cases.

Psychoneuroses are fundamentally psychogenic and develop in the midst and because of abnormal psychological experiences. Before discussing these experiences let us present a few examples of psychoneurotic manifestations.

One female patient, twenty-eight, following a normal confinement with no undue loss of blood and with a prompt recovery, misinterpreted her very slight serous vaginal discharges as due to a serious affection of her genitalia. Otherwise perfectly sound, she consulted a number of gynaecologists who treated her by various methods, and two of whom performed curetting.

The woman became depressed, She felt unhappy and was in constant fear of malignancy, physical or constitutional, without there being any actual basis for this thinking. Subsequent events proved that her belief was only psychogenic as she made a complete recovery under a psychotherapeutic management.

A young married woman, twenty-five, was suffering with chronic constipation, accompanied by occasional headaches. Coming frequently in contact with a female friend who also had headaches and who attempted to commit suicide in a fit of jealousy of her husband, my patient developed an idea that her friend became insane because of the pain in the head, and therefore her own headache might in the future lead to the same consequence.

She was in constant fear of such termination. She was advised to consult an oculist, who promptly refracted her eyes and told her that the proper glasses would cure the condition.

For two years she was in a state of fear and anxiety without witnessing any relief. She consulted a gynaecologist and also a general surgeon at different periods. The former curetted the uterus; the second operated for suspected adhesions of transverse colon. Neither the glasses, nor the curettment, nor the operation on the colon removed the original mental condition although everyone of the three men assured her that the removal of the condition, which they considered respectively as the sole morbid cause, would undoubtedly bring about a complete cure. Under psychotherapeutic measures during a short period of time the fear and anxiety as well as the slight headache had all disappeared.

A young man of twenty-five, during a three year period complained of disturbances referable to almost every organ in his body. At first it was the heart, then the gall-bladder, then the nasal cavities, the ears, the eyes, the genitalia, rectum and finally the right hypochondrium. Numerous physicians in and outside of hospitals were consulted and everyone advised and actually performed some manipulations or small operations. Some of them advised gross abdominal operations. For the latter of his multiple complaints a surgeon advised an appendectomy.

Accordingly the patient was placed on the operating table. While the preliminary preparations were being made, namely, the assortment of the instruments, washing the hands of those who were to participate in the operation, etc., the patient was suddenly seized with fear. He refused to be operated on and at once left the hospital. Since then there has been no return of pain in the right hypochondrium.

Toward the end of his peregrinations, he observed a slight cloudiness of his urine. At once he conceived the idea of a kidney affection. Again he consulted several internists, each of whom made a different diagnosis.

It must be mentioned at this juncture that during the entire illness, which lasted for several years, the patient continued uninterruptedly his usual occupation, namely, that of a railroad conductor. He always slept well and had a voracious appetite.

At the time of the examination there was no doubt in my mind as to the psychogenic origin of all the complaints of the patient. Psychotherapeutic management alone succeeded in removing the last obsessive ideas. He is well at present, but since such disorders are episodic in character the probabilities are, that new hypochondriacal manifestations will eventually make their appearance when confronted with new emotional factors, the nature of which will be discussed later.

A girl of seventeen developed abulic phenomena. If she noticed a loose brick on the ground, while crossing a street she would get frightened. She could not and would not step over the object, but would go around it and continue her gait. When, however, she would make an effort to overcome her deficient will power, she would tremble, cry and stop.

Being slender and pale and having irregular and scanty menstruation, she was taken first of all to a gynaecologist whose diagnosis was anteversion of the uterus and that the latter was the direct cause of her psychoneurosis. He urged an operation. A general surgeon, consulted subsequently, spoke of uterine adhesions and advised some surgical procedures, the nature of which this author could not determine. A laparotomy was performed with the result of a decided intensification of her psychic condition, as well as of her menstrual difficulties.

Discussion

Examples, such as the few related, could be multiplied, but they are sufficient to demonstrate that besides a physical there is also a psychological approach which, may be the most important, if not the only method in managing psychoneuroses. An

organic or structural lesion can no more be viewed as the sole basis of functional psychic disorders.

In order to know how to manage these peculiar phenomena, let us briefly consider their nature and their meaning.

The behavior of every individual is the result of an interrelation of several elements, namely, emotional instinctive tendencies, such as fear, anger, self-assertion, attachment, etc., plus the environmental conditions.

The instinctive tendencies will have a different coloring in different individuals, according to inherited qualifications. A highly or less sensitive person will manifest his or her emotional elements in different ways. The constant interaction between these instinctive emotions and environmental objects or occurrences produces complex psychological states or complexes.

We live, therefore, in the midst of daily or hourly conflicts between the inherent and exterior elements. Complexes are being created continually. When they are recognized by the individual self, the conscious ego is able to overcome them and the normal state is maintained and not disturbed. However, many of them are not recognized, and since all complexes are different from eachother and have a different aim and purpose, antagonism of one to another is constantly being created.

As these complexes are not recognized the conscious ego has no control over them, and they may remain with us for an indefinite period of time and are apt to create functional nervous disorders or psychoneuroses.

In fixed ideas, obsessions, fears, states of anxiety, abulias, etc., in all such cases, as we have seen from the histories of the few patients cited above, the physical symptoms alone emerge, such as pain in the hypochondrium simulating appendicitis, or pain in the cardiac or pulmonary region simulating a disease of the heart, of lung, etc. But the emotion associated with the fixed ideas remains, and as long as the latter is unaltered or not removed, the physical manifestation stays on and the patient will continue to feel unhappy.

The various physical manifestations of psychoneuroses may be relieved, and the individual may find with an effort on his part a certain skill in adapting himself to his environment and become more or less contented for the time being. But such a situation is not a cure, because the essential element in the conflict of various complexes has not been attacked, namely, the emotional instinctive factor, which plays the most important role in the psychoneuroses.

It is not only the adaptation to the environment, but also and more emphatically the adaptation to oneself that is important. Otherwise speaking, a psychoneurosis can be removed only when the sufferer is shown how to unravel and lay bare the elements of the complexes which are in constant conflict so that he can face himself.

Attempts to remove physical discomfort will not remove the emotional elements which have created the psychic discomfort and which the patient will continue carrying with him indefinitely.

The inability to understand this essential principle and the want of desire of considering a psychological end in human suffering besides a purely biological end, are the cause of failure of treatment. Therein lies the reason for the fact that quite frequently the cause of psychoneurotic disorders is sought elsewhere, in the uterus, ovaries—generally in the genitalia. Next in order is the digestive apparatus that is not infrequently incriminated. Dilation of the stomach, gastroptosis, enteroptosis, nephroptosis, and cholecystitis are all conditions that are thought of with major operations consequently being performed.

Not only is there total therapeutic failure as far as the patient's complaints are concerned, but undesirable local and general consequences may arise which will render the operated individual organically unfit in addition to his psychic unhappiness. As one of the many examples of this particular contention is the damage produced by castration in women.

In a paper read before the American Medical Association (Vol. LXIII, 1345) the medical histories of 113 women who underwent complete or partial removal of the uterus or ovaries or of both, were presented. They were discussed from the broadest standpoint by internists, general surgeons, gynecologists and neurologists.

It was shown that the preexisting nervous and psychic phenomena for which the operations were undertaken became aggravated in the weeks and the months following the operations. The obsessions and other psychoneuroses with which several women suffered prior to the oophorectomies became, since then, more persistent and covered a larger field of morbid ideas than heretofore.

These who suffered with hysterical paroxysms began to have them in a more accentuated form and more frequently. Former hypochondriacal and anxiety states became deeper. All such cases were referred to the gynaecologists with indiscriminate assurances that their vague nervous manifestations were exclusively due to indefinite gynaecological conditions.

Of course the operations were uniformly successful, but the victim's existence was rendered most unfortunate and distressing.

It was evident that partial or complete hysterooophorectomies disturbed the well established physiologic effect of ovarian tissue on the economy or perhaps disturbed the intimate relationship between various ductless glands which, as we have some reasons to believe, exist. At all events, in addition to the preexisting psychic phenomena additional disturbances were thus created.

The foregoing observations are sufficiently illustrative to contend that the real cause of psychoneurotic phenomena does not lie in accidental occurrences, such as traumatism, fatigue or local diseases,

etc. These factors react on us all daily, hourly, and do not produce disorders of a permanent nature.

A psychoneurotic individual on the contrary reacts differently because of the special make-up of his mental characteristics. The latter render him highly suggestive, highly sensitive, and highly emotional. While they do not present new phenomena which are not observed in normal individuals, their reaction, however, to all kinds of stimuli is expressed in a greater intensity and is reproduced with a greater facility and branches out in a most unexpected manner.

The complexes which were described above and which we consider as the result of conflicts between the instinctive emotional elements and the environmental occurrences are not easily recognized, and they are not properly interpreted when recognized by psychoneurotic personalities because of peculiar characteristics. The complexes which arise in them are more numerous, more antagonistic to eachother because of the greater intensity of each emotional element which enters into the formation of the complexes.

The environmental factors which also form a part of the complexes equally give a different sensorial impression in the psychoneurotics, and consequently the mental representation in the latter will correspondingly be different from that of normal individuals.

The methods employed in the management of psychoneuroses are several. The object of the present thesis is not the discussion of methods or procedures in bringing to the surface the modus operandi of the complexes which are the basis of psychoneurotic phenomena.

This doctor's main purpose is to call attention to the fact that all those abnormal manifestations are too psychic in character, that the functional disorders of which the victims complain are too much dependent upon special mental attitudes to be attributed exclusively to organic disorders of tissues and organs.

Psychoneurotics are psychopathic individuals. They occupy a place between insane and normal. Their number is legion and their multiple manifestations present infinite varieties and subvarieties. The latter are intermingled and mixed with human suffering in all its forms and degrees, medical as well as surgical.

In dealing with human life it behooves us medical men to approach its phenomena not only from a purely biological but also from a psychological standpoint. The former has for its object the adaptation of the individual to his environment. The latter is to have him adapted to himself. It is only after the latter task has been successfully accomplished that the individual will be fit to face his environment.

No removal of tissues or organs, no artificial correction of disturbances, no matter how accurately or skillfully they may be done, will succeed in making a psychoneurotic discard his fixed ideas, his hypochondriasis, his abulias, his fears or his obsessions. The person must be taught properly how to restore peace amidst the bewildering complexes.

Summary And Conclusion

The multiple varieties of psychoneurotic manifestations and their genesis are interpreted on the basis of conflicts between the instinctive emotional forces and the conscious ego. Their relationship to somatic disorders is illustrated by a few case histories.

The urgency of approaching human life, not only from a purely biological but also from a psychological standpoint, is stressed.

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Iowa Scientists Successful With "ADA" In Treatment of Ulcers

Four Iowa scientists performed a simple operation to test the effect of aluminum dihydroxyaminoacetate, called "ADA", on white rats having stomach ulcers.

Robert L. Dryer, Joseph Katz, Dr. J. I. Routh, and Dr. W. D. Paul, all of the University of Iowa staff, conducted the research. First all of the rats had been fed a balanced diet with vitamin supplements. The ulcers which resulted were apparently very similar to those which afflict humans, but were inevitably more severe.

Some of the rats developing such ulcers were treated with ADA, and some of them were not.

"In every case," says the Iowans' report, "ulceration was much less severe in rats receiving ADA. In a majority of cases ulcers were prevented."

If prepared for humans, the dose of ADA given the rats would be equivalent to the amount of medicine contained in two aspirin-size tablets. If the ADA treatment is found practical for humans, says Dryer, even this amount would probably be spread over a number of doses.

Ulcers seem to be associated with an excess of acid in the stomach. The Iowans say ADA shows great promise because it seems to have a double advantage.

The aluminum part of the ADA compound is formed by the body into an acid-neutralizing agent. The amino acid which is split off in this process acts as a buffer to tie up excess acid.

Editorials

PURKINJE—A Medical Pioneer

Among the great pioneers of modern scientific medicine, the name of *Johannes Evangeeista Purkinje* (1787-1869) of Bohemia, stands high. He was a pioneer in the use of the microscope and he obtained wonderful results from that somewhat crude instrument which was available. He also was a physiologist of genius, and his career is intensely interesting.

Like a great many Americans, he began his life as a teacher, then after having taken orders, graduated in medicine at Prague—his graduating theme being on *Subjective Visual Phenomena* which attracted the attention and gained the friendship of Goethe, who was himself the greatest plant morphologist of his day.

It is said that through Goethe's influence, Purkinje obtained the professorship of physiology and pathology at the University of Breslau.

Purkinje was a Slav and racial prejudices were strong in that part of Germany, which means that he was received coldly. However, he soon lived down this racial aversion by his modesty and superior knowledge. He remained at Breslau almost thirty years where he gained both fame and golden opinion. He was called to the chair of physiology at Prague. At Breslau, he did notable work in the development of German medical science; indeed, he was the founder of laboratory teaching in German universities.

He and his pupils did such outstanding work in an attic of his own house in which he had a laboratory, that the Prussian Government built him a Physiological Institute. As was the case with Carl Ludwig, some of the treatises of Purkinje's pupils represented the ideas of the master. He pointed the way in the use of the microscope. He was the first to use the microtome, Canada balsum glacial acetic acid and the Drummond line light.

Purkinje was a discoverer in more than one field and was greatly interested in ophthalmology. He wrote with Gabriel Valentin, the celebrated essay on ciliary epithelial motion. They described, what are now known as the, "Purkinje fibers" of the cardiac muscle and of the uterus. Purkinje was a physiologist of quite extraordinary range, and likewise a good pharmacologist.

In regard to clinical medicine, he was the first to study vertigo and rolling of the eyes, which was produced by rotating the erect body in a vertical axis. It is true that he did not connect this phenomenon with the semicircular canals, but his description may be termed as the starting point of modern work on vestibular and cerebellar nystagmus.

Duke Elder, the author of a *Textbook of Ophthalmology* refers to Purkinje as one of the most brilliant observers of subjective phenomena, and also he points out that the rich treasury of Purkinje's three great works remains unsifted for the most part. He also remarks that his history of tragedy does not stand alone in the annals of science.

In the beginning of Purkinje's medical and scientific research work, he labored in the attic of his house, in which the equipment was necessarily scanty, but where he did his original work. When presented with a wonderful state Physiological Institute, originality seemed to depart, proving that the true spirit of science rarely shines in an atmosphere of luxury. However, there may be an alternative explanation, as temperament and racial temperament may have played a part.

Some brilliant men come to the full powers of intellect early; they work intensively and then these powers appear to fade. The Latins and Slavs, as a rule, are of this type. They mature more rapidly, physically and mentally, and seem to become more or less worn out at a comparatively early age. The Teuton and Scandinavian stock, on the other hand, are perhaps generally less brilliant, at any rate they mature more slowly, and they last longer. Climate has an influence on the development of physical and mental powers, and it is likely that a temperate climate is most favorable for the lasting of the brain's power. Who can say?

Carlyle's definition of genius as 'an infinite capacity for taking pains' does not sound true. Intuition is a leading factor in genius, particularly when the possessor of this has a sane mind in a sound body. So many men of genius have been erratic in mind and diseased in body.

Purkinje was a genius and physically strong, but his mental powers appeared to wane at an early age.

Post-Traumatic Conversion Hysteria Held Compensable Against Charge of Malingering

In a proceeding under the New Jersey Workmen's Compensation Act the main question on appeal from an award by the Compensation Bureau of 100 percent disability after a previous award of disability of 25 percent, was whether the employee had suffered increased disability subsequent to the original award, or whether he was a malingerer.

The employee had suffered four separate accidental injuries while in the respondent's employ, all affecting the region of his lower back, one after another. They were tried together resulting in an award of 25 percent partial permanent disability consisting largely, upon the basis of both orthopedic and neurological findings, of a lumbar-sacral and "sacroiliac sprain involving the nerve roots" as well as "accelerating and aggravating underlying arthritic conditions."

The award for increased disability was entered four years later, finding the man 100 percent disabled, largely because of a severe conversion hysteria or psychoneurosis of a posttraumatic nature.

Lay, orthopedic and neurological testimony for both parties was presented. The court merely said that if the facts testified to were true the award of 100 percent total permanent disability was amply justified. If they were not true the award would not be justified.

The court did not find that any of the doctors testifying would say that the man was a malingerer. The court holds it to be definitely settled that psychoneurosis and conversion hysteria are quite real and may well result from industrial accidents.

It has been held, Vaccaro vs. Walter Kidde & Co., 144 N. J. L. 491, 48 A. 2d 393, that an employee's blindness was the consequence of psychoneurosis of the conversion hysteria type and that "hysterical amblyopia is well known to the science of neurology."

Whether a man is a malingerer or not, the court concluded, "can only be ascertained with the greatest difficulty by those who have the opportunity and the skill to observe him properly. When those who have observed him, including the physician appearing for the respondent, are unwilling to term him a malingerer, it would be asking much of this court, which has never had the opportunity to observe him, to reach this very conclusion.

". . . For in the face of the determination to the contrary of the Bureau, which did have the opportunity to observe him and hear him, there is nothing in the record which *per se* indicates that he was neither telling, nor acting, the truth." That being the case, the award was affirmed. Watts vs. City of Newark, New Jersey Court of Common Pleas. 54 A. 2d 6-22.

Medical Information And The Public

In the *Annual Report*, of the work of the New York Academy of Medicine for 1946, there are so many items of general interest that the data have been used by certain magazines and newspapers, notably the *New York Times* in commendation of the efforts of *liaison* between medical and non-medical readers.

The printed brochure contains over 80 pages, and all of them are worthy of careful reading, but our attention descended particularly upon the section which tells of the work of the "Committee on Medical Information." This committee is under the chairmanship of Dr. Harold R. Mixell who has made the "story" of great general interest.

Following cessation of hostilities, it seems quite natural that in the business of "getting back to work", information was sought in twice the volume which was maintained during 1945 when we were barely beginning to emerge from the long shadow of devastating War.

Some 5000 inquiries were dealt with by the Bureau, one-fifth of them from physicians. Another fifth came from the press, two-fifths from non-medical persons ("lay individuals"), and a remainder from miscellaneous sources such as business, certain "organizations", governmental agencies and the like. Statistically, there were 1500 letters; 3200 telephone calls; and 550 interviews.

Eighty-one manuscripts were submitted from various sources for analysis with a view to publication, and 312 "radio talks" were checked before delivery. That represents an enormous amount of detail, and calls for 24 hour service.

We are told that various members of this Bureau have been awakened from sleep at times to "clear the deck" for some excited reporter who thinks he has a "scoop" or a "thriller" right in his hand. Like the legend about the Post Office, neither hail nor rain nor snow nor any earthly thing prevents these "couriers" from doing their job. It is, indeed, a labor of love, and is recompensed chiefly by the knowledge that a real service is being rendered to humanity. It is as real as that of the bedside or operating room.

Three categories represent the classification of the kind of work performed. First is the press, radio, and their relation to the general public. Second, there is the information of public "goings on" at The Academy, such as the addresses of the President of the Academy, the "papers" read before certain sections or during the Graduate Fortnight, and Memorial Lectures such as the Salmon series.

The matter of "ethics" appears whenever a physician wishes to write or read an essay for public consumption and still conform to the "Principles" as set down in the code. A third category deals with laity lectures, health education conferences, and participation by the Committee, or some of its mem-

bers in discussions of common interest to medical and non-medical persons alike.

Teachers, social workers, nurses, health workers of all grades, and students of sociology or economics have "problems" the solution for which is sought at The Academy.

It is interesting to note that certain publications make requests for review of manuscripts. There were 81 such requests during 1946. The list includes *Cosmopolitan Magazine, Readers Digest, Colliers, Coronet, Parents Magazine, Look,* and *Science.* No censorship is exercised in any of these instances.

Chief thought is given to accuracy of statement, and the attempt is made to see that the vast reading, (and radio) public is correctly informed on health matters. The Journals value these services highly, and occasionally offer tribute, voluntarily of course, to the Academy treasury. Those consulted often find "problems" where writers are confused, overenthusiastic or downright careless about accuracy or truth, of the material they offer for publication. Many who write about psychiatry without intimate knowledge of this vast subject, seem to be in a fog, and are, therefore, dangerous as exponents of fact.

Advertizing agencies, one is pleased to note, sometimes consult the Bureau in the interest of accuracy. One can hope that they do so more often and adhere more closely to honest findings than seems to be the case. It would be, in this connection, interesting to find out how much truth there is in "statements from doctors" as to the non-irritating properties of this or that cigaret, or somebody's special coffee.

This writer is often annoyed by the frequent use of doctors as a body to bolster up claims which must be, at least, only half truths. And so it is good to know that the National Better Business Bureau, the Federal Trade Commission and other like organizations call upon the Bureau to evaluate their advertising copy. Both staff and consultants must necessarily give a great deal of time to this phase of the work.

Under Laity Lectures, items were: The Role of the Medical Man in War; The Atom in Medicine; Are Parents Necessary?; Anti-Infectious Agents of Natural Origin, and American Pioneering in Psychiatry.

Attendance here was from 250 to 700. There were motion pictures to illustrate certain lectures, and a question period at the close which stimulated interest and released further information. The New York City Station, WNYC, broadcast most of the lectures, and the newspapers carry advance information to the prospective audiences.

The 1946 Annual Health Education Conference was devoted to "Biology Instruction at the High School Level," which has long been a theme for speculation and controversy, some of it bitter in content. It came to light that there is widespread dissatisfaction with subject matter and methods of instruction, and a better way or ways is being sought to bring "the facts of life" to the adolescent without stimulating sex consciousness or the desire to experiment with the knowledge thus acquired.

A film called "Shock" was presented for opinion, and in the judgment of many psychiatrists it was condemned as a means of teaching the facts concerning mental ill health, and the way to recovery. Condemnatory judgments were transmitted to Mr. Eric Johnston of the motion picture industry.

There is much more of interest in the Report of the Committee, but these "samples" shall have to suffice. We, who live in New York City may well be proud of the comprehensive work of our Academy.

The Care of the Aged

A survey committee on the problems of ageing and the care of old people under the chairmanship of *Dr. Seebohm Rowntree* recently has reported its conclusions. The problems of old age are among the most obvious and serious besetting Britain at the present time. Statistics show that they are not only urgent but are at an increasing rate.

The *Rowntree* research exposes ruthlessly and nakedly facts, which hitherto have been hidden. Their significance had been glossed over. Now exact knowledge is being made public.

The *Rowntree Report* is a model of research technique. It provides a contrast indeed to various publications issued of late purporting to deal with social problems but evading facts and based largely on reported anecdotes and their authors' views.

No facts, but suggestions and conclusions in plenty.

Here, the reader is informed whence and how the facts were obtained and the views of the committee as to the validity, more or less general, of each set of facts.

As for conclusions, they are deduced logically from the facts published, and the somewhat few suggestions arise from these conclusions. The committee has done its work thoroughly, blending library research and field work skillfully—the secret of real social investigation.

Members of the committee visited forty-eight

homes and institutions in various parts of Britain and started field surveys in ten different areas. No fewer than 2,300 old persons were visited and the results thereof were recorded in questionnaires which were sorted out and tabulated.

In every civilized country there are large numbers of old and elderly persons but in none are they as numerous as in Britain. It is obvious that they are not an asset except in comparatively few instances. On the other hand many, if not most of them, have served their country ably in their active life and deserve to end their days restfully. If poor and sick, as well as aged, their plight is sorrowful and needs aid.

Many generous and prompt plans have been and are being suggested with this end in view. Some have been carried into effect but much more must be done ere the problem is even solved partially. Other countries have a surplus of old, elderly and sick. In fact, it is largely an international question.

In this country more prosperous in most ways than any European or Asiatic country, and which has not endured the stress and strain and the destruction wrought by war, that is, not within her own borders, she has her old, elderly and chronically sick but no doubt the matter has received due consideration and will be attended to in a fitting way.

Quackery in Bygone Times

It may be true in some of its meanings that, 'where ignorance is bliss 'tis folly to be wise', but it does not apply to science or medical science. For example, when ignorance was universal many abuses existed and flourished which have been killed by the advance of science. Among the medical sciences which have done away with many abuses, quackery was not the least.

Quackery has been universal from time immemorial and this high sounding phrase is true. Coleridge's aphorism, "The best inspirer of hope is the best physician" has been employed by charlatans and faith healers throughout the ages and it seems now that this principle is to have a definite footing as psychotherapy.

Medical practice during the Renaissance period was impregnated with superstition, herb doctoring and what would now be termed quackery of every kind. The great British surgeon, William Clowes (1540-1604) characterized the horde of wandering cataract couchers, lithotomists as no better than renegades and vagabonds.

In Britain there were many successful charlatans of both sexes. Sir William Read (?-1715) was among these. He flourished as an oculist in the time of Queen Anne. Someone wrote an eye book under his name while a Grub Street poet praised him and his treatment in doggrel verse. He found it more profitable to prey upon the gullibility of the public and pretending to mend their eye affections than making or mending clothes.

Ignorant but shrewd, he was successful and was hailed by some of his patients as the possessor of almost magical knowledge and skill. Queen Anne had defective eyesight which rendered her peculiarly susceptible to the wiles of imposters of all kinds and especially so to those who posed as eye specialists. He gained her favor and was knighted. Afterwards he became oculist to George I.

Chevalier Taylor was the most picturesque of all the British quacks. He, like Read, posed as an oculist. He was either the son of a female apothecary in Norwich, England, or according to Dr. R. Rutson James, F. R. C. S., son of a Norwich medical practitioner. He described keratoconus, that is after Dudden had described it, operated successfully for squint where others had failed, worked with Cheselden at St. Thomas's Hospital, London, invented a cataract needle and other instruments and among his numerous publications was *Mechanism of the Eye* in 1750.

It may be mentioned here that Daviel, the Frenchman and the originator of the modern treatment of cataract by excision of the lens, in the early part of his career was a roving oculist, who sounded his own praises as the wandering medieval eye-couchers used to blow their own trumpets. Chevalier Taylor impressed Handel and Gibbon with his skill and perhaps, it may be said, his pattern but Dr. Johnson and Horace Walpole were impervious to his wiles. Walpole was a sceptic and a cynic and Dr. Johnson was endowed with more than his share of hard common sense.

Joshua Ward, known as "Spot" Ward because of a claret colored mark on one side of his face was a very successful charlatan. General Churchill, afterwards Duke of Marlborough, was among his most enthusiastic patrons. He won the confidence of George II by reducing a dislocated thumb.

Quackery was extinguished practically when the medical profession and the general public became better educated. When the quacks thrived it was not only on account of the deep ignorance of the people at large, even the rich and supposedly well educated were ignorant of any little medical science, but because the mass of the medical profession itself were devoid more or less of real knowledge of medical science. When the profession became alive to the need of science, its members entered into its study and practice with vigor and it was not long before quackery was swept away by the incoming of true science.

MEDICAL ESSAY

Where Is The Individual?

B. LIBER
New York

Intelligent, broadminded and generous people have a profound respect for the individual. He is a part of and a product of world society. He also has a share—however small—in shaping those personalities with whom he lives, his circle, his group, his class, nation or country and, indirectly, humanity as a whole. Not only exceptional and outstanding persons have this effect and influence, but anybody, no matter how insignificant.

From the ideal point of view it is important for social progress that the individual be respected, that he live a fairly comfortable life and that he be physically and mentally healthy. Not only for his own sake, but also for the benefit of his close and more distant neighborhood, it is necessary that he be given the opportunity to develop as much independent thinking as possible and that he enjoy as much freedom as it is compatible with his adjustment to other individuals.

The words *individuality* and *personality* are almost synonymous and interchangeable. Individuality limits the person in the midst of a group and reveals him or her as distinguished from the rest. Personality emphasizes the character and the mentality which originate and radiate from an integrated being—body plus mind. It is not redundant to speak of the personality of an individual.

We are all aware of the fact that no two individuals—men or animals or even plants—are perfectly identical.

Some time ago this writer, in his studies of twins, followed two geminate siblings, whom only the mother was able to tell physically apart. After some time one could notice a slight dissimilarity here and there and even then one was uncertain whether this was actually present in the anatomy as such or in the way the organs were used.

These twins were fourteen months old and their incisor teeth were equal. But the mouth of one of them assumed some lines that were unlike those of the other infant. The skin around the eyes also varied slightly. But whatever real difference existed between them was incomparably more outspoken in their mental aspect—in their behavior, understanding, response and reaction, that is, in their personalities.

One baby laughed easily and was amused by anything she saw. The other was serious and observed people and objects attentively. Her smile could be provoked only after some effort and it disappeared quickly. One moved her arms and hands gaily in the air. The other was quieter and more deliberate in her motions.

The steps of one baby around the park bench or around their double carriage seemed to be exactly like those of her sister. Both grabbed the boards or the wheels with precision and held on powerfully and in the same manner. One reached her aim faster because she stopped only from time to time, while the other discontinued her promenade often and for long intervals to contemplate and examine her surroundings.

At a given moment the mother sat them both down and offered them some fruit juice. Both refused it, but one of them took the bottle and, with a wonderful and cheerful expression on her face, she tried to smash it against the edge of the vehicle, while the other paid no attention to the bottle.

At this point the mother produced an apple out of her bag, peeled it and cut it into small portions. She presented a piece to one baby and told her to say "tah-tah". With a contented, acquiescing giggle the child repeated these sounds immediately and directed the fruit toward the mouth. She wanted another piece and got it after willingly pronouncing the magic syllables.

The other child craved the apple. She stretched out an arm toward it, but when told that she must say, "tah-tah" first, she wagged her head vigorously. As the desired thing was resolutely denied to her, she cried bitterly and shook her entire body, firmly opposed to the slavish utterance of the password. Finally the mother, vanquished, handed her the piece of apple and then another and another. And only after complete satisfaction a smile appeared on her face and, without anybody's orders, she voluntarily said, "tah-tah".

There is no doubt that these children, mentally already so distinct from one another, will soon have little in common. *They will be almost the same individuals with two unrelated personalities.* They were born with different inclinations. As they go on in life, each one will mold what she will absorb from the world into her own mental needs. Within a short time their behavior will be poles apart from eachother—even more so if society will give them an opportunity to mature according to their own qualities.

What, within the individual, strikes us as the most conspicuous and characteristic part? What do we love, what do we despise in a person? Why does a superb Adonis often choose a squat, freckled woman? Why does, not so seldom, a fleshy, buxom, voluptuous, or even a physically graceful female prefer a bow-legged, pitiful-looking male? (Was not one of Aphrodite's husbands the lame and limping, but skillful Hephaistos?) Because of the brainy attributes, the sunny brightness, the intellectual power, yes, and the mental beauty of the apparently abnormal choice.

A great orator speaks with all he has, with his sonorous, winning voice, his perfect diction and his convincing arguments; but also with his body, his limbs, his gestures, the fire in his eyes. Yet, when we think of him later, only what he said and how he said it stands out eminently. Indeed, we do not even need to know him or to see him. Reading him may be enough. His physique disappears and is concealed behind his excellent mentality except perhaps in a large part of his female audience which often cannot admire without falling in love.

Friendship through a sort of platonic correspondence may be purer, loftier than through direct acquaintance, because it allows our imagination to lead us—though it may mislead us instead, which is not always a misfortune. We become familiar with a mind and clothe it with whatever body we wish. The fact that a friend of this writer, never seen and living at the antipodes, whose real age was eighty-six, gave in his energetic letters the impression that he was thirty, did not hurt anyone. For all intents and purposes he was thirty.

What is worth while in the individual? Surely not those functions or even qualities which he shares with everybody else. Not the performances which he has in common with others such as, eating, breathing, and sleeping. Not one inch forward would have ever been made if we, as individuals, had not come out, some more, some less, from the ranks, from the beaten path, and had not distinguished ourselves in one way or another.

What is significant in us is not our similarity but our *dissimilarity*. Even under abnormal conditions, when mentally ill, our illness differs according to our personalities. The instruction referring to any ailment, "do not treat the disease, treat the patient" is always true.

But where is the individual?

It is only partly to be found in the nervous system, in the endocrine chain, in the alimentary tract, and so forth. Most of the corporal work is *automatic*. We have no power to command our heart to start or to stop its beats. We cannot discontinue our respiration for any length of time. We may refuse to eat, but once we have swallowed, digestion, assimilation, takes place without our consent or willpower. Even some of our thoughts just happen, or are connected with facts and events outside ourselves and they make us laugh or cry with others.

There is of course a difference—however slight—between the organs and functions of human creatures. But the great difference between one person and another lies in the thinking process and it would be even more prominent if we were permitted to fully develop our originality—that is where the individual dwells.

65 West 95 Street

News Items

Denver Scientists Increase Use of Rats for Experimentation.—A critical nationwide shortage of laboratory animals, particularly dogs, for medical research has been highlighted by an announcement from the University of Denver by Doctors Fred D'Amour and Frank R. Blood who have developed methods and miniature instruments which enable rats to be used in some research and instruction formerly requiring dogs and cats because of their larger size. Their techniques are reported in a new manual to be published by the University of Chicago Press.

Since rats have a less developed central nervous system, they cannot replace dogs for many experiments. The rat has a substantially different digestive system than both the dog and man and they do not react to many drugs in the same way that higher animals do. Also, the rat has 7 to 10 times as much skin surface in proportion to body weight as man and has a much higher respiration rate which make animals more similar to man in these respects essential for many tests.

Schering's 1948 Subject Award Title is Announced.—The subject of "The Role of Hormones in the Maintenance of Pregnancy", is the basis for the Schering Award for 1948. For the three best manuscripts submitted by undergraduate students of American and Canadian medical schools on such a designated phase of endocrinology, the Schering Award annually awards cash prizes of $500, $300, and $200.

Army Nurse Reports on Pacific Picture.—Lieut. Col. Ruby F. Bryant, who has seen two years of service as director of nurses for the U. S. Army Far East Command, revealed in her report that living and working conditions among her sister officers in Japan are on the whole favorable. She informed Col. Mary G. Phillips, director of the Army Nurse Corps that notwithstanding housing and certain other problems the large majority of nurses on duty in the Orient are happy and enjoying their tour of duty both professionally and socially. These factors lend much encouragement to the task of sending 300 nurses to Far East Command to relieve those who have completed two years overseas service.

Britain Receives Fresh Eggs From the U. S.—The Food Parcel Clinic, of Overseas Inc., 136 West 22 Street, N. Y. reports that business firms now can ship fresh eggs to their colleagues in Great Britain. The eggs are sent in specially constructed crates, and air mails three dozen of them for $7.95. Through its special foreign agents abroad it was reported that eggs have been consistent number one request. The ration overseas is only one egg a week, and most parents have been giving their meager share to the children and getting none themselves. Overseas Associates also ship hams, turkey, butter, jams and jellies, shortening, salad oil and hundreds of other most needed foodstuffs to Britain and the Continent.

Markle Foundation Appoints First Group of Scholars.—Sixteen young scientists have been appointed as the first group of scholars in medical science under the plan announced last fall by the John and Mary R. Markle Foundation to support qualified scientists who wish to make a career in academic medicine. The scholars were selected from candidates nominated by accredited medical schools in the United States and Canada by regional committees appointed by the Foundation. Toward the support of the scholars and their research, the Foundation has allocated a total of $400,000 to their respective medical schools, each school to receive $25,000 payable at the rate of $5,000 annually for five years.

These new appointees will be faculty members of the participating medical schools devoting the next five years to teaching and research, at the end of which time they will have had an opportunity to become established teachers and investigators.

Hotel Pennsylvania Plays Host to Occupational Therapists.—The 31st annual convention of the American Occupational Therapy Association, will be held in the Hotel Pennsylvania, N. Y., September 8 to 11.

Blain New Medical Director of A.P.A.—Dr. Daniel Blain, formerly with the Veterans Administration as head of its psychiatric division, has been appointed the new medical director of the American Psychiatric Association. This association, through its new leadership, expects to take a bigger part in legislative matters, publish literature with popular appeal and otherwise extend its influence. Dr. Blain however, will remain chairman of the department of neuropsychiatry at Georgetown University School of Medicine.

Cornell Celebrates 50th Anniversary.—March 11, marked the 50th anniversary of the Cornell University Medical College. In celebration the day included a series of clinics, conferences and demonstrations in the College and Hospital Buildings. The scientific exhibit proved to be of special interest for it displayed 180 research projects now being conducted at the Center. Among these were exhibits in psychosomatic medicine, including gastric function and the relation of nasal function to life situations; new work in streptomycin; new developments in experimental surgery and in anesthesia.

Chemist Discusses Sex Hormones.—"The Chemistry and Physiology of Sex Hormones," was discussed at the chemistry colloquium of the Research laboratories at Brown University, Providence, recently by Dr. Erwin Schwenk, director of chemical research, Schering. The interrelationship of the endocrines and their dependence upon each other, their chemistry, and the physiologic effect of these hormones on human tissue was presented together with the historical aspects of endocrinology.

Dr. Schwenk is well known as a leader in the development of alpha estradiol, the pure ovarian follicular hormone; the male hormone, testosterone; and other important products.

Parran To Investigate Needs for Children's Fund.—An intensive study in China, the Philippines, Indonesia and other oriental lands—the investigative grounds for the International Children's Emergency Fund, is on the *future list* of Dr. Thomas Parran, whose duties will cease April 6 as surgeon general of USPHS. Formal announcement of his decision to undertake the investigation is expected shortly. The trip will require about two months and Dr. Parran will make the study of children's health problems for ICEF, a United Nations organization, while on a leave status from USPHS.

Hawaii Medical Service Membership Could Be "Upped" To 100,000.—Among the outstanding points brought out in the discussion by Allen B. Thompson, vice president of Associated Hospital Service—New York's Blue Cross Plan at a recent meeting of hospital directors and physicians in Honolulu, was that the present membership of an estimated 20,000 persons in Hawaii Medical Service Association could be increased to more than 100,000 by the end of this year provided that specific modifications of policy and procedure were instituted.

Mr. Thompson's foremost suggestion was that greater emphasis should be made upon meeting the high costs of hospital and medical care, rather than provision of comprehensive home and office care for relatively small fees.

He went on to say that the long-term hospital illness, combined with surgical or medical care in the hospital, constitutes the greatest economic health hazard and urged serious consideration of revisions aimed at protecting the public against catastrophic expenses incident to sickness.

United Medical Service Increases Benefits.—As a result of favorable experience throughout 1947, benefits granted to United Medical Service members on a temporary basis have become a continuing feature of the organization's surgical and surgical-medical plans. In addition, the amount paid to physicians for normal obstetrical delivery on behalf of UMS members enrolled in the surgical plan has been increased from $60 to $75.

The United Medical Service, which is sponsored by the Medical Society of the State of New York and 17 county medical societies, now entitles members to specified payments for medical care in the hospital beginning with the first day of admission instead of the fourth day. The maximum payments for each hospital admission comprise $200.50 as against a former maximum of $182.50.

Personals

Dr. Woodrow M. Morris is the newly assigned assistant professor of clinical psychology and senior psychologist at the psychopathic hospital, State University of Iowa. Dr. Morris formerly served as director and chief psychologist, Division of Special Clinical Services, Bureau of Psychological Services, Institute of Human Relations, University of Michigan.

Chief of the Veterans Administration pharmacy division, *Dr. W. Paul Briggs,* has resigned his position. Dr. Briggs who had been with VA since March, 1946, established a home-town pharmacy program and has improved the calibre of pharmacy service in VA hospitals, homes and regional offices.

In addition the doctor developed a procedure for the selection of drugs used in VA hospitals and homes by creating standing committees on therapeutic agents in each VA field station. An Executive Committee on Therapeutic Agents was formed in the central office, Washington, D. C., with Dr. Briggs as secretary, to coordinate the operations of the field committees.

Dr. Neil P. Macphail is the recipient of the fifth annual presentation of the Richard P. Strong medal for outstanding service in the field of tropical medicine. Doctor Macphail, veteran surgeon and sanitarian of the United Fruit Company, Quirigua, Guatemala, has been active in this field since 1907, when fresh from Scotland he accepted a position as quarantine doctor for the plague-ridden port of Belize, British Honduras.

Dean Thorndike Saville, New York University College of Engineering, was appointed by Governor Thomas E. Dewey to serve on the Public Health Council until January 1, 1953, which is the unexpired term of the late Henry Neely Ogden. Dean Saville has held his present post at the University since 1936 and he is a member of numerous scientific and engineering societies.

The two American scientists who were invited to attend the symposium at the National Center of Scientific Research, Paris, France recently were *Dr. Richard H. Barnes,* director of Biochemical Research, Medical Research Division, Sharp & Dohme, Inc., and *Dr. Erwin Chargaff,* professor in the department of chemistry, College of Physicians and Surgeons, Columbia University.

Dr. Barnes discussed his paper written in collaboration with Dr. Samuel Gurin, Department of Physiological Chemistry, University of Pennsylvania, on "The Formation and Utilization of Ketone Bodies."

This symposium is one of a number being organized by the National Center of Scientific Research, a branch of the French Ministry of Education. The symposia are supported by grants from the Rockefeller Foundation.

Dr. Clyde W. Geiter has assumed his duties as medical director of the George A. Breon & Co., having been formerly associated with Frederick Stearns & Co., as industrial physician. Dr. Geiter is well known, along with Dr. Parker Heath, professor of ophthalmology of the Post Graduate School, Harvard, for the introduction of Neo-Synephrine HCL. in the eye field. He discovered and made Neo-Synephrine Sulfathiazole, a bacteriostatic vaso-constrictor.

John F. McCormack has been appointed executive vice-president of United Medical Service to facilitate joint activities of the organization and its affiliate, Associate Hospital Service—New York's Blue Cross Plan. He is also a past-president of the New York State Hospital Association, the Greater New York Hospital Association, and the Hospital Bureau of Standards and Supplies.

Nationally-known orthopedic surgeon and closely identified with the reorganization of medical care in Veterans Administration hospitals, *Dr. Paul B. Magnuson,* was named chief medical director for VA. Dr. Magnuson, former professor of surgery and chairman of the Department of Bone and Joint Surgery, Northwestern University Medical School, Chicago, succeeds Dr. Paul R. Hawley, who resigned January 1. However Dr. Hawley is now serving the VA administration as special assistant and advisor on medical problems.

In addition to his job with the VA, Dr. Magnuson is associated with the Passavant Memorial hospital, Chicago, as attending surgeon and is senior consulting orthopedic surgeon, Wesley Memorial hospital, Chicago. He also is civilian consultant to the surgeon general of the department of the Army.

Dr. Maurice L. Tainter, director and *Dr. W. Dexter Bellamy,* research bacteriologist of the Sterling-Winthrop Research Institute, Rensselaer, N. Y. have been elected to fellowship in the New York Academy of Sciences, which is the fourth oldest in the country and has more than 4,000 members.

Recognition was extended to Dr. Bellamy for research on vitamin B6, particularly in regard to the function of this vitamin as a co-enzyme. His current interest is antibiotics.

Dr. Ilza Veith has been selected consultant to the Army Medical Library to work in the field of oriental medicine. She received her Ph.D. in the History of Medicine from Johns Hopkins University, and has published a number of articles dealing with historical and medico-historical problems of the Far East. Her assignment includes surveying the present holdings in oriental medicine and making recommendations for purchase and assisting in reference problems and in cataloging the backlog collection.

LETTER FROM BRITAIN

(From Our Own Correspondent)

Affairs, lay and medical, are progressing at a rate in this country which some think is too rapid and that real progress cannot be gained in such a manner. On the other hand advance means change and if change is represented by forward movement then it is, or may be for the benefit of all.

The medical profession, that is its members, is in a state of expectation. Some of the members look forward hopefully, while others are satisfied with existing conditions and view the future distrustfully. But, from whatever viewpoint the situation is regarded, the most sensible attitude is to anticipate coming events cheerfully—not in regard to the shadows they cast. Such is the philosophy of the wise.

Salaries of Anesthetists in Middlesex

Middlesex County Council has increased the original rate of pay for anesthetists from £1000 (about $5000) a year by £50 (about $250) yearly up to £1,400 (about $7,000). The amended scale rises from £1000 a year by £100 (about $500) to £1,600 (about $8,000) a year and after proof of outstanding achievement by further increments of £50 (about $250) to £1,800 (about $9,000).

The Nursing Situation in Britain

The situation as regards nursing in Britain is curious. It seems that the publicly provided hospitals are so short of nursing staffs that a considerable proportion of their wards have had to be closed. On the other hand, the big voluntary hospitals still have waiting lists while the total number of nurses qualifying has risen appreciably since pre-war days from 9,000 to 13,000 per annum.

This state of affairs, or crisis is attributed partly to lack of funds provided to make hospitals independent or more or less so. Miss Nightingale placed great store on the fact that her school at St. Thomas' Hospital, London, had enough money to ensure adequacy of staff for teaching and adequacy of accommodation. However, this is quite a partial explanation of the situation and it appears that many reforms are needed and that test examinations for would-be entrants will not nearly solve the problem, even if they do not make its solution more difficult.

Art in Medicine

Miss Anna Zinkeissen, artist to St. Mary's Hospital, Reddington, London, is exhibiting at the time of writing at Foyle's Bookshop, Charing Cross Road, medical pictures. Most phases of treatment are depicted with acute observation but with due restraint.

The exhibition includes pathological drawings lent by the Royal College of Surgeons. This may be a move in the right direction and in keeping with the times. It is said that other hospitals here are toying with this novel departure and may follow suit.

Humphry-Davy Rolleston Lectures

On July 15, Professor P. C. P. Clarke will deliver the Humphry-Davy Rolleston Lectures at Royal College of Physicians Home in London. His subject will be, "The Treatment of Disseminated Sclerosis by Artificial Pyrexia and Prolonged Administration of Arsenic."

Sir Clive Forster-Cooper, F. R. S.—Dead

Sir Clive Forster-Cooper, F. R. S. director of the Natural History Department of the British Museum is dead. Born in London in 1880, he was educated at Rugby School and Trinity College, Cambridge, where he became interested in zoology.

He joined the staff of the North Sea Fisheries Commission Research Establishment, spending a year in the service mostly at sea in a converted trawler. After he had joined another expedition to learn more of the marine biology of the Seychelles he took up the study of fossil mammals introduced to this subject by Dr. C. W. Andrews, with whom he went on an expedition to the Fayum Egyptian desert to study its fauna. On his return from Egypt Forster-Cooper visited the United States to view the immense collections of fossil mammals in the American museums, more complete than any in Europe.

He spent a year in the American Museum of Natural History working under H. F. Osborn. He was associated in New York with W. D. Matthews, W. K. Gregory, Barnum Brown and Walter Granger, paleontologists who, with Osborn, according to an obituary of Forster-Cooper in *Nature* September 24, did much to establish our knowledge of the history of mammals on a firm foundation.

On his return to Cambridge he was awarded the Balfour studentship and made two dangerous but successful expeditions to Baluchistan in 1910 and 1911 collecting there, and later preparing and describing the extraordinary rhinoceros Baluchithesium—the largest of all land mammals. He had become active in the preparation of fossils and of most museum arts and in 1914 was appointed director of the Cambridge University Museum of Zoology.

He spent the war period until 1918 on malaria, and became a Fellow and bursar of Trinity Hall and in turn was largely responsible for the building of the new Cambridge University Library. In 1938 Sir Cooper was appointed director of the British Museum (Natural History). When the second great war broke out his plans for the improvement of the Museum were cancelled.

He was a great zoologist, a man of great culture, a good draughtsman, an excellent water color painter and etcher and, like many great men—modest and shy.

Woman Health Minister

A health minister in the person of Miss Mabel Howard has been appointed to the New Zealand Cabinet. She is the first woman to be given such a post in an English speaking country.

Book Reviews

Obstetrics

Principals and Practice of Obstetrics: By JOSEPH B. DELEE, M. D., late professor of obstetrics and gynecology, University of Chicago; consultant in obstetrics, Chicago Lying-in Hospital and Dispensary; and J. P. GREENHILL, M. D., attending obstetrician and gynecologist, Michael Reese Hospital; obstetrician and gynecologist, Associate Staff, Chicago Lying-in Hospital; Chairman Dept. of Gynecology, Cook County Hospital; professor of gynecology, Cook County Graduate School of Medicine. Ninth edition. 1108 illustrations on 860 figures, 211 in color. Philadelphia and London: W. B. Saunders Co., 1947. Pp. 1011. Price $10.00. Kugel.

This edition has been rewritten and new chapters added on: Minor disturbances of pregnancy, premature labor, prolonged pregnancy or postmaturity, missed labor, fetal erythroblastosis and prematurity. The chapters on analgesia and anesthesia have been revised with due consideration to methods of preventing neonatal disturbances.

Part I is concerned with: The physiology of reproduction, labor and puerperium; Part II deals with: The pathology of pregnancy, labor and puerperium.

The physiology of reproduction and development of the ovum has been brought up-to-date and clarified by colorful illustrations. The physiology of pregnancy evaluates the metabolic mechanisms affecting all systems of the body. Conduct of pregnancy is presented from the standpoint of the practitioner. Physiology of labor offers the principles of engineering and the effects of labor on the child's organism. Obstetric and gynecologic endocrinopathies reveal the current chemical as well as the clinical concepts. Pathology of pregnancy stresses the common disorders and their management.

Painstaking details are given in the chapters on operative obstetrics emphasizing pitfalls in methods of delivery. The book remains a veritable mine of information with pertinent illustrations on every aspect of obstetrics.

Social Pediatrics

Child and Adolescent Life in Health and Disease—A Study in Pediatrics: By W. S. CRAIG, B. Sc., M. D., professor of Pediatrics and Child Health, The University of Leeds; physician-in-charge, The Children's Department, The General Infirmary at Leeds. Edinburgh, Scotland: E. & S. Livingsone Ltd., 1946. Pp. xvi + 667. Price $7.00.

This author believes this book on social pediatrics to be the first of its kind. No doubt there have been many books of social history; but this is the social history of children, the children of the poor in our country from the beginning of the industrial era to the present day. It describes how the children of the poor have fared in the transition of a small agricultural nation to a large and crowded industrial society; and the successive efforts made by individuals, groups and the State to mitigate the condition of destitute, homeless and disabled children.

The whole range of human needs throughout the span of child and adolescent life is covered, and how these needs have been supplied from 1600 to 1945 is clearly described. Such is the subject of Dr. Craig's book; and it is immense both in its range and complexity; and no less in its importance.

The story opens with the provision of what was called *Relief for the Poor,* within and without institutions, in the Poor Law Act of Elizabeth, 1601. Institutional care was then given to young and old alike in the same buildings, later to be called Workhouses. It was nearly a hundred years later when the foundation of Orphanages began the removal of these children from the Workhouses to more humane institutional care and when some of the sick children of the poor were admitted to the early General Hospitals. It was later still when the miserable fate of abandoned newly born infants led to the creation of Foundling Hospitals, where for many years they continued to die in such large numbers that a writer, commenting on the published death rates of the Foundling Hospitals of London and Dublin about 1790, declared that these institutions had the aspect of charnel houses rather than hospitals.

The industrial era was now in full swing.

Destitution diminished; but poverty remained, and to it were added the evils of massed epidemics of disease among children in the houses of the working poor, and the employment of children in mines and factories. These conditions roused further the social conscience both of individuals and of the community. Reforms and remedies dealing with every phase of life in childhood and adolescence were begun and were slowly extended.

Thus education of the child, begun in "ragged" and factory schools about 1790, only became a national system in the Education Act of 1870. And the first organized medical care of infants in Dr Armstrong's London Dispensary for the Infant Poor, in 1769, had to wait until 1840 when the publication of statistical records of infant mortality at last unmasked this gigantic problem of infancy. But it took eighty years more of private and public effort to get a national scheme of care in the Maternity and Child Welfare Act of 1918.

Oliver Goldsmith pronounced a poet's judgment on these conditions in the DESERTED VILLAGE; contrasting village and city life, and putting wealth in the scales against human lives, he wrote:

"Ill fares the land, to hast'ning ills a prey,
When wealth accumulates and men decay."

The first part of Dr. Craig's book is a full commentary and confirmation of the truth of the poet's words.

In the second part of his book, he passes from history to a detailed account of the care of the child and adolescent in health and disease as it is practiced today. He describes the clinical machine at work in the home, the clinic, the hospital and many other institutions; the directing mechanism of administration; and the laws which sanction all these activities.

This book creates a picture, for through a full text and numerous illustrations it crystallizes the great range and importance of the subject of child

and adolescent life, and the interlocked character of the many problems that compose the whole.

Dr. Craig is not so much concerned to enlarge on the faults and deficiencies, as to give the facts. With these facts clinicians and administrators, social workers and social architects can now see the whole problem and bring it under critical review. After reading his book no one can be satisfied with our social and medical services dealing with children. They have many of the marks of the second-rate-overlapping and duplication of work; incoordination and mistiming of the different services; unfriendly rivalry of authorities working in the same field; poor training of doctors, midwives and nurses in child medicine, and particularly in regard to child health; and the overhead load of bad housing conditions.

The book ought to be read by everyone concerned with the care of children and adolescents, by all teachers of doctors, midwives and nurses who practice child care, and by all who devise and control the machinery of administration.

Dr. Craig's story of child neglect in the past; and his account of the disconnected services of child and adolescent care at the present time ought to break down all complacency. He draws attention to at least two general lines of reform—a linking up of the disconnected clinical services, and improvement in the basic training of all who conduct these services. His book supplies the facts necessary for a constructive discussion, and a bold execution of reform.

These facts are more important and more powerful than eloquent pronouncements. They throw a searching light on the past and the present; and their light falls also on the path of the future. They are a guide as well as a call to drastic action which can hasten the reversal of Oliver Goldsmith's scathing judgment. We shall then accumulate and no longer squander that source of national wealth which lies in the health of children and adolescents.

Practical Treatment of Pharmacology

Pharmacology, Therapeutics and Prescription Writing. For Students and Practitioners: By Walter Arthur Bastedo, Ph. G., Ph. M. (Hon.), M. D., Sc. D. (Hon.), F. A. C. P., consulting physician, St. Luke's Hospital, N. Y.; St. Vincent's Hospital, Staten Island, and the Staten Island Hospital; president, U. S. P. Convention 1930-40; member revision committee, U. S. P.; formerly curator of the N. Y. Botanical Garden; attending physician, City Hospital, N. Y.; instructor in pharmacology, Cornell University; associate in pharmacology and therapeutics and assistant clinical professor of medicine, Columbia University. Fifth edition. 82 illustrations. Philadelphia and London: W. B. Saunders Co., 1947. Pp. 840. Price $8.50.

This new addition maintains the tradition of presenting pharmacology in terms of clinical medicine and conforming to the *United States Pharmacopeia*. A great variety of new material has been included especially amino acids, the blood fractions, coagulants and anticoagulants, heparin, dicumarol, curare, snake venoms, analeptics, antihistamines, convulsants and anticonvulsants, folic acid, rutin, thiouracil and its derivatives, sulfonamides, penicillin, streptomycin, demerol, metopon, the cardiac glycosides, the antimalarials, the mercury diuretics and the BAL treatment of poisoning by arsenic, gold and other substances.

Under each individual remedy there is a clear summary of the features of the drug, solubility, various methods of action, manner of prescription and administration, indications and contraindications and toxicity from the standpoint of symptoms and treatment.

The book is a practical compendium of remedies in action. The final chapter is devoted to prescription writing emphasizing the use of individual drugs rather than proprietory products. With the many advances in therapeutics this new edition is indispensable in everyday practice.

Applied Allergy

Allergy in Theory and Practice: By Robert A. Cooke, M. D., attending physician and director of the department of allergy, Roosevelt Hospital, New York, N. Y. Written in collaboration with thirteen contributors. With 43 illustrations. Philadelphia and London: W. B. Saunders Co., 1947. Pp. xxv + 572. Price $8.00

This delightful monograph by Dr. Cooke and several New York allergists is an outcome of a cooperative venture in postgraduate teaching. It includes an integrated series of didactic lectures on theory and practice of allergy sponsored by the American College of Physicians in previous years.

The book records the clinical facts and synthesizes recent advances for everyday practice in spite of the intricacies of its immunologic phases.

In undergraduate instruction allergy is an essential part of the basic sciences of immunology, bacteriology, pathology, pharmacology and physiology. Immunology cannot be taught without a discussion of sensitization in the experimental animal (anaphylaxis) and in man. Therefore, the author opens the book with the principles of this phenomenon and its applicability in human disease. This, supplemented by laboratory descriptions of shock and of precipitin, of the *Schultz-Dale* reaction and of passive transfer skin tests, form the basis on which the study of allergy is gradually developed.

With the aforementioned introduction, the medical student comes to his clinical work with a foundation that permits a ready grasp of those various diseases for which allergic reactions, in whole or in part, are responsible. Later these basic facts and theories are coordinated with clinical diseases such as tuberculosis, syphilis, rheumatic fever and those of the erythema group, as well as asthma, urticaria, serum disease and the manifestations of drug allergy.

Graduate instruction divides itself into the early years of interne training and the later extended work in residencies and fellowships. The usual two years of medical internship should be devoted primarily to the basic field of internal medicine or pediatrics, but a rotation possibly by election, through the various clinics dealing with the medical subspecialties as allergy, diabetes, hematology and cardiology would exert a wholesome and broadening influence.

In a properly organized allergy department an intern could profitably spend one or two months and gain clinical and technical experience of great value, particularly useful for those who go immediately into general practice where problems in allergy will present themselves in at least 7 to 10 percent of the patients. Physicians so trained will know how to undertake the study and treatment of such cases at least in their simpler form. With an occasional short and properly sponsored postgraduate course of the "refresher" type which is available, these practitioners will be able to render greater and more capable service to their communities.

The organization of the book is ideal for ready reference or contemplative reading. After preliminary chapters on the fundamental aspects of allergy the author discusses allergy of the bronchi, the upper respiratory tract, of the skin, nervous system, spine, cardiovascular system and of all other systems of the body in which clinical manifestations appear. There is an excellent discussion of allergens in relation to allergic disease and on clinical and laboratory procedures in the diagnosis of allergic disease.

Allergic phenomena in children are discussed, especially bone scoring, diagnostic procedures, special system manifestations and practical therapy. The material was written by 14 allergists, yet the book is a well integrated unit reflecting Cooke's plan.

Each chapter presents not only the theoretical and clinical but also a terse summary and pertinent references to recent literature. There have been many books on allergy in recent years but this is the least verbose and the most authoritative.

One of the main difficulties in the assemblage of this monograph is the emphasis on theory rather than practice. To be sure the theory embodies interpretations now universally accepted but it does not help sufficiently the actual management of each of the allergic diseases. The allergic manifestations in infants and children are a little different than those seen in adults except for the degree of chronicity. Nevertheless, the chapter on pediatric allergy is limited to differential diagnosis of asthma and gastrointestinal allergy.

This imbalance reflects the primary interest of the particular author rather than the predominant group of conditions that might have been included.

Cardiovascular Diseases

Cardiovascular Diseases: By DAVID SCHERF, M. D., associate professor of medicine, New York Medical College, Flower and Fifth Avenue Hospitals and LINN J. BOYD, M. D., professor of medicine, New York Medical College, Flower and Fifth Avenue Hospitals. With 56 illustrations. Philadelphia, London and Montreal: J. B. Lippincott Co., 1947. Pp. xviii + 478. Price $10.00.

This is a completely new book although it is based on former editions, which were favorably received and translated into seven languages. The authors admit that the important subject of rheumatic fever with heart complications was inadequately treated by them hitherto.

The doctors follow the general aversion to citing streptococcal infections as the potent cause, preferring to ascribe it to "allergy or some related state." But in writing the chapter on *Subacute Bacterial Endocarditis*, which is certainly found frequently with the rheumatic fever syndrome, they are pleased to note that there is a steady increase of patients who have been "cured" by penicillin.

Regarding coronary sclerosis which bids fair to become "the doctor's disease", atherosclerosis is regarded as synonymous. The deposit of cholesterol esters in the intima plus lime salts causes proliferation, thickening and terminal occlusion of the coronary arteries thus bringing about the well-known symptoms of pain, heart block, myocarditis, and eventually death.

Ingestion of large quantities of eggs and milk favor excessive deposits of cholesterol—according to Dock and his followers, but Scherf and Boyd have found quantities of cholesterol or its crystals in the pericardial fluid with a normal blood level of cholesterol! However, it is said that, "Very little is known about cholesterol metabolism." It is certainly high time that research institutions be established where such matters can be intimately studied, so that the growing menace of cardiac disease be checked.

The heart under x-ray study has references in several places, but this examination seems to have more to do with deviations in size than with other conditions such as rhythm.

This is an excellent book in helping to understand cardiac pathology, but we have many such. We need to know more about prevention.

Histopathology of ENT

Histopathology of the Ear, Nose and Throat: By ANDREW A. EGGSTON, B. S., M. D., director of Laboratories, Manhattan Eye, Ear and Throat Hospital; clinical professor of Pathology (Post Graduate Division) New York University Medical College; director of Laboratories of The Mount Vernon Hospital; pathologist, Harlem Eye and Ear Hospital; DOROTHY WOLFF, A. B., M. A., Ph. D., research investigator, Endaural Hospital, New York City, fellow in Research, Harvard Medical School. Illustrated. Baltimore, Md.: The Williams and Wilkins Co., 1947. Pp. viii + 1080. Price. $18.00.

Dr. Eggston has spent a lifetime in getting together the data for this remarkable work. He has been ably assisted, not only by his co-author, but by many physicians both in and out of hospitals.

The book covers the entire field of histopathology of the ENT field. Moreover, the material is so presented that the reader obtains an excellent idea of both the physiologic and pathologic processes which exist side by side in the same person.

Each section of the book begins with comparative anatomy of the organ under consideration, and the basic sciences of embryology and histology. With this background, one is ready for the changes which disease works upon the special organs in relation to the general body economy. This is intended to be a book for reference, but it is much more than that because of its clinical significance in relation to office and bedside daily practice.

SURGICAL DIGEST

By RICHARD A. LEONARDO, M. D.
Rochester, N. Y.

Treatment of Decubitus Ulcers Conway *et al.* have had successful results with the plastic closure of decubitus ulcers in paraplegic patients by excision of the ulcer and simple closure (when possible) or by closure with pedicled flap, or by skin grafts, etc. All these chronic ulcers failed to respond to conservative measures. The authors state that their best results were obtained in those cases where a flap of skin and its subcutaneous tissue from a neighboring area is applied to the site of the excised decubitus ulcer and the donor site is covered by a free skin graft.

Exstrophy of the Bladder C. C. Higgins studied 41 cases of exstrophy of the bladder and believes that these infants should be operated upon before their first birthday, since to delay operation endangers the kidneys unnecessarily. He performs a modification of the Coffey I technic, implanting the ureters into the sigmoid colon. The exstrophic bladder is excised at this same sitting, but any necessary plastic work on the penis is postponed for four or five years. About 20 percent died, but many of the remaining patients have been well and free of symptoms for the past five to ten years.

Hodgkin's Disease John H. Talbott treated a series of cases of Hodgkin's disease with nitrogen mustard as well as with radiotherapy. It is his opinion that nitrogen mustard does not produce superior results to radiotherapy in the average case of this disease. There are others, however, who claim improvement after radiotherapy has no longer seemed worthwhile giving to many of these cases. In all instances permanent cures are not so much to be expected as is a general clinical improvement and a remission in the progress of this disease.

Prophylactic Chemotherapy for Acute Appendicitis When penicillin and the sulfa drugs are given routinely to patients with acute appendicitis, both preoperatively (only one dose usually, while waiting for a free operating room) and postoperatively, Griffin *et al.* found that the operative mortality and the postoperative morbidity were greatly reduced by this prophylactic chemotherapy. They studied 108 consecutive cases at the Cook County Hospital, Chicago, and compared the results of that series (mortality only one percent) with the mortality of the other series wherein the mortality varied from three percent to seven percent, or more. Now, no one has to be convinced of the prophylactic value of such therapy.

Renal Tuberculosis From his studies on about one hundred cases, C. P. Mathé finds that this condition occurs less often in the Western part of this country; that coincident renal calculus was present in seven percent of the cases; that if the lesion is unilateral, the mortality is barely over one percent; and that over one-third of the patients nephrectomized had ureteral stricture. Mathé, therefore, feels that close postoperative supervision is of the utmost importance.

Cancer of the Tongue About one-third of these cases can be converted into five-year cures by x-ray therapy combined with interstitial radium applications, according to Sharp and Spickerman. Prompt biopsy of early lesions is of distinct help in the prognosis as it affords the patient adequate treatment before metastases occur. Penicillin and the sulfa drugs are also given for any secondary infection that is present and that might otherwise lead to dissemination of the cancer cells to other parts of the mouth.

Reiter's Syndrome According to Young and McEwen, this syndrome (characterized by the presence of arthritis, non-specific urethritis, and conjunctivitis) is but an unusual complication of bacillary dysentery. They are apparently the first American authors to offer case records in proof of their contention that Reiter's syndrome. Instead of being a distinct etiologic entity, it is simply a complication of bacillary dysentery. They proved their cases by history and by finding positive agglutination titers for Shigella organisms in several of their cases.

Serum or Infectious Hepatitis Any hepatitis occurring within six months of a blood or plasma transfusion is apt to be this disease. We now realize the use of pooled blood or serum is not without danger, as many of these patients with homologous serum jaundice fail to recover; and no blood should be taken from a prospective donor if he gives a definite history of jaundice. In the differential diagnosis, one must eliminate stone or stricture or malignancy of the common bile duct, lesions of the head of the pancreas (especially cancer), or malignancy of the ampulla of Vater.

Cavernous Sinus Thrombosis Surgery may be needed to excise or incise and drain the origin of this infection, but the treatment of this infection itself should be conservative. Recent investigations show that best results are obtained by the early use of anticoagulants (heparin and dicumarol) in conjunction with adequate doses of the sulfa drugs and/or of the antibiotics, especially penicillin or streptomycin, depending on the identification of the causative organism.

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MARCH, 1948

Medicolegal Notes

Causal Connection Where Two Successive Injuries Are Concerned

In a Massachusetts Workmen's Compensation proceeding, the sole contention of the employer, a self insurer, was that the evidence was insufficient to prove that the disability claimed was due to an injury sustained on January 5, 1945, rather than to a prior injury sustained on December 4, 1943.

In the first accident the employee's hand was caught in a riveting machine, fracturing the fifth metacarpal bone and the proximal phalanges of the little and middle fingers, and lacerating all the fingers and the palm of the hand. The fractures were reduced and his wounds sutured. Later there was an open reduction of the fracture of the middle finger and a bone plate was inserted. The employee returned to work which did not require the use of the right hand.

The second injury occurred when a spark got into the glove on his right hand while he was grinding metal chips on an emery wheel and in attempting to knock off the glove he struck the hand against the machine, again fracturing the fifth metacarpal bone and apparently causing some disturbance of the bone plate on his middle finger.

He was paid compensation for nine months after the second accident when he returned to work, but again quit work five weeks later because of pain after removal and loosening of screws on the bone plate. These were removed by an impartial physician, whose report concluded with the statement that "his present condition would seem causally related to both accidents but it is impossible to say which one played the major part, probably the first." The employee later worked as a helper on a truck since February, 1946.

The Compensation Board found that he was entitled to compensation for total incapacity from October 12, 1945, to February 4, 1946, and for partial incapacity thereafter, and specific compensation for the loss of the use of the middle finger. This was sustained on appeal by the Massachusetts Supreme Judicial Court, Morin's Case, 72 N. E. 2d 406, citing several prior Massachusetts decisions.

The court said, "The employee had sustained two injuries of a compensable nature, and the insurer on the risk at the time of the second injury must be held liable to pay compensation for an incapacity following that injury where there is a causal connection between that injury and the incapacity, although the earlier injury may have been a contributing cause or even the major contributing cause."

Aggravation or Acceleration of Hernia Held Compensable

In considering the evidence, on appeal from an award of the State Industrial Board denying compensation, the Indiana Appellate Court recognizes the well established rule that it will not disturb a finding of fact made by the Industrial Board unless the evidence with all inferences reasonably deducible therefrom is of such conclusive nature as to force a contrary conclusion.

"Indiana," the court says, Heflin vs. Red Front Cash & Carry Stores, Inc., 73 N. E. 2d 494, 496, "long ago adopted the majority rule, that where an employee afflicted with disease receives a personal injury under such circumstances that he might have obtained compensation under a Workmen's Compensation Act on account of the injury had there been no disease involved, but the disease is materially aggravated or accelerated by the injury, resulting in disability or death earlier than would otherwise have occurred, and the disability or death does not result from the disease alone progressing naturally as it would have done under ordinary conditions, but the injury, aggravating and accelerating its progress, materially contributes to hasten its culmination, in disability or death, there may be an award under the Workmen's Compensation Act."

In Haskell and Barker Car Co. vs. Brown (1918)

67 Ind. App. 178, 117 N. E. 555, the word "accident" as used in the Indiana Workmen's Compensation Act was defined as "any unlooked for mishap or untoward event not expected or designed."

In Indiana Creek Coal & Mining Co. vs. Calvert, (1918) 68 Ind. App. 474, 119 N. E. 519, 120 N. E. 709, the Indiana Appellate Court, after an exhaustive review of English and American cases, approved the Haskell definition and further held the term "personal injury" as used in the Act, had reference not to some break in some part of the body or some wound thereon, but rather to the consequences or disability that results therefrom.

Applying these principles the court held in the Heflin case that a grocery store manager, whose hernia began to pain him, while he was unloading some 100 pound potato sacks, suffered a compensable injury from an "accident arising out of and in the course of his employment" where the evidence led inescapably to the conclusion that the injury materially accelerated the hernia, resulting in a disability earlier than otherwise would have occurred.

Essential Basis of Medical Expert's Opinion

In Indiana the Industrial Board is the exclusive trier of the facts in proceedings before it, under the State Workman's Compensation Act. Therefore the Indiana Appellate Court will not, on appeal from the Board's granting or denial of awards to claimants, weigh the evidence, if it is conflicting, nor attempt to substitute its judgment as to what facts have been proved and what facts have not been proved for the judgment of the Board.

But an award of the Board must be supported by competent evidence of probative value. If the evidence is of such a conclusive character as to force a conclusion contrary to that reached by the Board, then duty devolves upon the Appellate Court to reverse or set aside the Board's award because of the insufficiency of the evidence to sustain the award.

The Indiana Appellate court applied these rules in an appeal before it of an award of the Industrial Board of compensation to an employee for injuries resulting from an accident arising out of and in the course of the employment, and revised the Board's award, holding that the record conclusively showed that the employee claimant was entitled to compensation.

The Board was instructed to set aside the award, and to enter an award in favor of the employee in accordance with its opinion. Wright vs. Peabody Cord Co., 73 N. E. 2d 692. The opinion of the Appellate Court is to the following effect:

In this case two medical witnesses detailed the facts found by each of them during their physical examination of the claimant's back, and the opinion expressed by each of them was based upon such facts.

Three other medical witnesses testified for the

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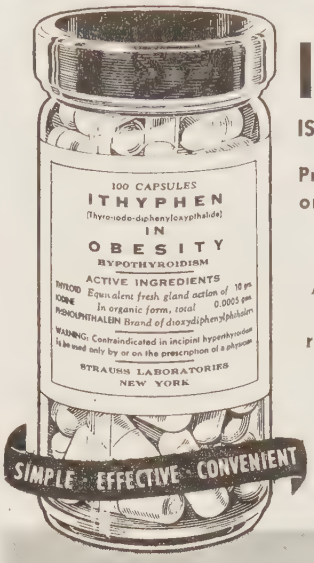

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employer. Their testimony showed that neither of them made a physical examination of the employee's back in the lower lumbar region to determine whether or not he was actually suffering from a ruptured intervertebral disc or discs, and none of them expressed an opinion in answer to a hypothetical question containing facts which the evidence in the case tended to prove.

"It is fundamental", the court said, "that the opinion expressed by a medical expert witness must be predicated on facts which the evidence in the case tends to prove, stated hypothetically or from personal observation. Otherwise such opinion has no probative value as evidence."

The court was forced to conclude, after carefully considering the testimony of these three medical witnesses that the opinion expressed by each of them was without probative value. Summing up, the court held that the evidence having probative value was without conflict, and the evidence to the contrary, tested by the above rules, was so conclusive in its character as to force a conclusion contrary to that arrived at by the Industrial Board and entitle the claimant to compensation.

Right of Cross-Examination of Witnesses Before Administrative Tribunals

The New York Court of Appeals has never held that, the right to cross-examine a witness is less when the hearing is before the administrative board than it is before a court.

Friedel vs. Board of Regents, 73 N. E. 2d 545, 547. "Cross-examination of adverse witnesses", the court says (p. 547), "is a matter of right in every trial of a disputed issue of fact. That right has always been enforced by this court, and by its predecessors from earliest times. That right, of course, can be exercised before administrative fact-finding tribunals, and denial thereof by such tribunal is error of law. But once the right has been accorded, the extent of cross-examination rests largely in the discretion of the tribunal, whose exercise thereof is not reviewable unless abused.

"It is clear, in any event, that before administrative tribunals as before courts, in the State, the right of the party is no more than 'to cross-examine to a reasonable extent.' Matter of Greenbaum vs. Bingham, 201 N. Y. 343, 347, 94 N. E. 853. Unless there is a plain abuse of discretion, limitation is for the quasijudicial tribunal, and the courts may not revise such a reasonable limitation, any more than they can revise any other such discretionary doings."

Applying these principles in a proceeding to suspend a license to practice medicine for alleged performance of criminal abortions, the Court of Appeals held that a subcommittee of grievances did not abuse its discretion in limiting the cross-examinations of investigators for the Board of Regents.

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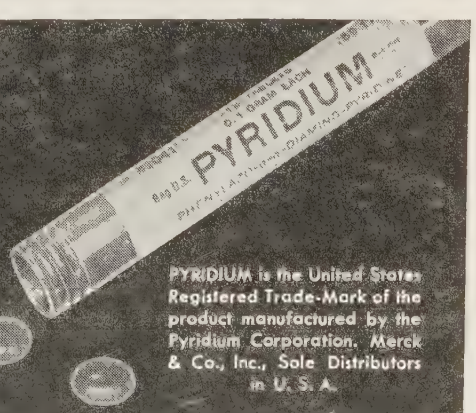

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Denver Lab Research Favors Testing With Rats

Experimentation with rats, in most kinds of endocrine study where organ removal is necessary, has proven to be superior over dog research as currently revealed by Dr. Fred D'Amour, director of the bureau of physical and biological research, University of Denver, and chairman of the Denver University department of zoology, and Dr. Frank R. Blood, associate professor of chemistry, Denver University.

These two men, authors of the "Manual for Laboratory Work in Mammalian Physiology", illustrate the superiority of using rats over other animals because the results are more valid, rats are easier to handle, their background and heredity can be more controlled, they require less room, are less expensive, and generations develop more rapidly. The rat has been standardized while dogs have not.

Doctor D'Amour's work on hormone assays have led to the adoption of standardized methods of determining and expressing the potency of hormones used in medicine thus assuring the patient and his physicians of products having uniform and dependable activity. His study of the Black Widow spider resulted in the development of a preparation and use of an anti-serum against her bite.

The most recent work that the doctor was involved in was recording the physiology of the rat at high altitudes which has led to an investigation of the efficacy of various means of artificial respiration and respiratory stimulants at high altitudes. This study, now underway, is being supported by a grant from the U. S. Navy.

International Surgical Assembly To Be Held In Rome

At the invitation of the Italian Government, Rome will be the scene of the Sixth International Assembly of the International College of Surgeons, during the week of May 16 to 23, under the presidency of Professors Raffaele Bastianelli, Raffaele Paolucci, and Mario Dogliotti.

The drawn-up agenda includes scientific meetings, scientific and commercial exhibits, visits to the Universities of Turin and Milan, together with tours embracing other medical centers in Europe. The highlighted featured exhibit will be the display of ancient texts on surgery which is being arranged by Davide Giordano, professor in Venice. This unique showing will be in the Vallicelliana Library in one of the historical buildings of the Vatican.

Since attendance is not limited to the membership of the College, all surgeons in good standing in their medical organizations are invited. Detailed information can be received by writing to Dr. Max Thorek, 850 Irving Park Road, Chicago 13.

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Western Reserve Initiates Microbiology Department

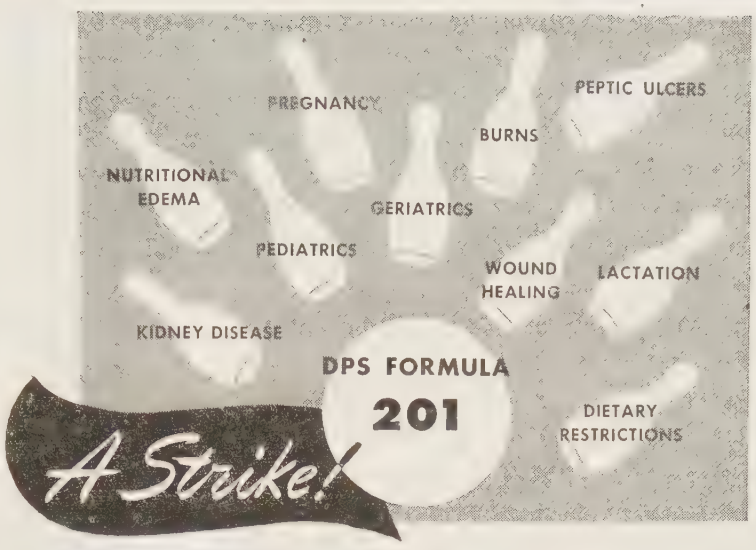
Recognizing the growing importance of the chemistry, physiology and biology of bacteria and other microorganisms, both in the cause and cure of disease, Western Reserve University has set up a department of microbiology in the School of Medicine.

Dr. Lester O. Krampitz has been promoted from the position of associate professor of biochemistry in the department of biochemistry, to head the new department as professor of microbiology.

The new department follows the recognition of the School of Medicine of the fundamental importance of the chemistry and physiology of the cell, whether it is a part of a human being or animal or unit of such microscopic or submicroscopic organisms as the virus, fungus, rickettsia, or bacteria. In addition to the department of biochemistry, several departments in the School of Medicine, including anatomy, physiology and pathology, are giving greater emphasis to the chemistry of the cell.

Dr. Krampitz pointed out that the growing emphasis on the chemistry and physiology of cells of microorganisms is in marked contrast with the more classical methods of bacteriology which have emphasized the relationships of morphology and taxonomy of bacteria to disease.

"Not so long ago", he said, "research scientists were reluctant to compare the chemistry and physiology of cells that make up the bodies of animals and man



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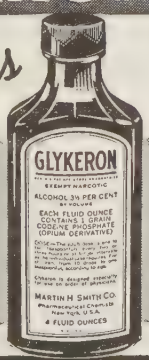
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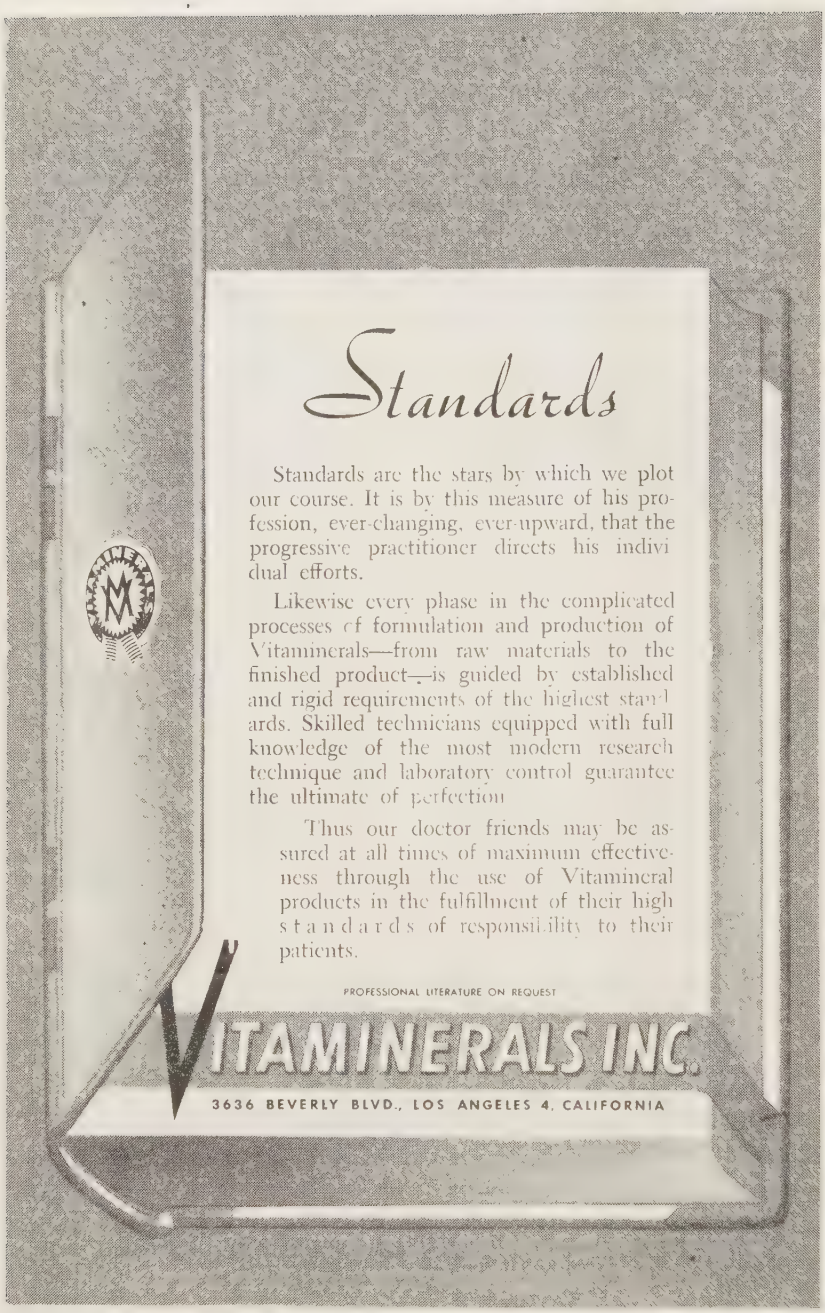
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with the cells of bacteria. Today, however, striking resemblances have been brought to light. These resemblances are leading to increased knowledge of life and the forces that destroy it".

The chemistry of microorganisms is stimulating the activity of the organic chemist in his efforts to make better and more effective drugs and other products synthetically, Dr. Krampitz pointed out. He gave as examples two important products of the chemistry of microorganisms—penicillin produced by a fungus, and streptomycin, the product of bacteria originally found in the soil.

"In studying the fundamentals of microbiology we will be more concerned with the activity of microorganisms than their morphology, which was emphasized in the past," he commented. "We will study the life processes of the organisms and attempt to determine how these processes affect host-parasite relationships."

"Biochemistry, whether in microbiology or in some other department of the School of Medicine, is a tool that is helping all medical sciences. We want to know what the events are that occur in cells and how other cells affect them."

He has found that penicillin, in its destructive action on bacteria, interferes with the "nucleic acid" metabolism of these microorganisms. Having demonstrated that penicillin interferes with the breakdown of nucleic acid—an important compound for the multiplication of bacterial cells. He is attempting to discover the mechanism of this interference.

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Life Insurance Institute Reports On Volume of Trade

Ninety-five out of 100 applicants for life insurance obtain policies, the Institute of Life Insurance reports. This is indicated by an analysis of one year's applications of companies representing approximately one-half of all ordinary life insurance purchased. The study, just concluded, shows that over 95 percent of the applicants received policies, 85 percent being standard rate policies and 10 percent extra rate policies.

Fewer than 5 percent did not secure the life insurance they applied for, and these failed to qualify chiefly because of serious physical impairments. Heart trouble and high blood pressure constituted the chief causes of uninsurability, together accounting for one-half of all the cases. Overweight was another important cause.

Fewer than one-half of 1 percent of all persons applying for insurance failed to obtain it because of underwriting qualifications other than physical, including occupation, location of residence, application for too much life insurance relative to income, habits, or excessive drinking.

"The percentage of life insurance applicants who secure policies has been increased in recent years," the Institute said, "as a result of experience gained through the careful screening of applicants made by all life insurance companies. These companies would like to insure every applicant. They exert every effort to extend the benefits of life insurance protection to as many as possible. But in the interests of the existing policyholders, they must set up certain standards to avoid accepting applicants with a probability of high mortality.

"At the same time, applicants with minor impairments have benefitted by the careful screening. Certain conditions which formerly were uninsurable may now be classed as warranting issuance of policies. Many of these cases require an extra premium, but in some of them policies may now be issued at standard rates.

"Outstanding progress has been made in connection with the issuance of policies to persons with certain physical impairments. Recent developments, especially the use of the electrocardiogram, have enabled the companies to accept many persons with minor heart conditions including certain types of murmurs and other heart impairments.

"Life insurance has also been made available to a limited degree to diabetics in recent years and on an even broader basis to those whose urinalysis shows a limited degree of sugar, whereas both of these types of persons were formerly turned down.

"In the aggregate, many thousands of persons annually secure life insurance today who were uninsurable only a relatively few years ago, and this has been made possible by the companies' continuous research into possible means of extending coverage to more people.

"Every life insurance applicant is checked on such matters as family history, actual physical condition, occupation, habits, and amount applied for in relation to income. A century of underwriting experience has shown that certain conditions preclude the issuance of life insurance policies. Excessive overweight is one of these. Several companies have experimented, seeking to classify excessively overweight applicants, with a view to finding certain types that are insurable at standard rates, but have as yet been unsuccessful. As the degree of overweight increases, the mortality hazard invariably increases.

"Another factor which has an apparent close tie to insurability is the ratio of the amount of insurance applied for to the income of the applicant. Almost invariably the companies have found that where this ratio is excessively great the mortality is excessive.

"Occupation has a very definite relation to insurability and executives appear to have a greater than average handicap. In some company checks, they have been found to have several times as many physical impairments as average applicants.

"Height and body measurements have been found a valuable additional check on general health, as there is a relationship between these measurements and weights, which is an important pointer to health."

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Announcing Penicillin Nasal Aerosol—Premo

Latest of the Premo specialties on penicillin administration is the penicillin nasal aerosol-premo, with penicillin nebutabs (each containing 50,000 units of crystalline penicillin sodium G) and penicillin nasal nebulizer (positive and negative pressure).

Indicated in sinusitis where a penicillin-sensitive organism is involved, the penicillin nasal aerosol-premo represents one of the most efficient, compact and easily portable nebulizers.

The penicillin nasal aerosol-premo has been accepted by the Council on Physical Medicine of the American Medical Association.

Beckman MX-5 Radiation Meter Announced

The growth of atomic energy projects and the expanding use of radioactive substances have developed a need for better instruments to detect and measure radioactivity. Recognizing this need, National Technical Laboratories, South Pasadena, Calif., manufacturers of Beckman pH Meters and other Beckman instruments, has developed several portable radiation instruments.

Recently announced is the Beckman Model MX-5 Radiation Meter, a portable Geiger-Muller counter weighing only 9 pounds, for the detection and measurement of X, beta, and gamma radiations. It is ideal for the measurement of radioactivity of low intensity, such as locating isolated radioactivity leaks or lost radioactive materials in factories and industrial applications . . . for mineralogical surveys . . . for checking apparatus and equipment for contamination by small amounts of radioactive materials . . . for following the course of tracer elements and other radioactive materials of low intensity . . . and for laboratory and experimental work. Since the instrument, including the GM tube, is completely waterproofed, and the case is desiccated, it is excellent for use in humid climates, in wet weather and on board ships.

The MX-5 Meter is battery operated, with the self-quenching GM tube mounted on a three foot probe. A selector switch gives three operating ranges, 20, 2 and 0.2 mr/hr. The MX-5's new type circuit eliminates zero control, features rapid meter response and extends battery life to 400 hours.

An external control to compensate for changes in battery voltage and tube characteristics permits calibration under any operating condition. The aluminum case has a smooth hard finish and all external surfaces are made of material not easily contaminated.

Pansulfa—Triple Sulfonamide Suspension

Description: A palatable liquid combining microcrystalline sulfathiazole, sulfadiazine, and sulfamerazine in 1:1:1 ratio. Each 5 cc. teaspoonful contains 0.5 Gm. (7½ grs.) combined sulfonamides.

Action: Bacteriostatic—inhibits the growth of certain pathogenic organisms, notably hemolytic streptococci, staphylococci, pneumococci, meningococci, Proteus vulgaris, E. coli and Pseudomonas aeruginosa. Provides a greater margin of safety in sulfonamide therapy. By limiting the concentration of any one of the sulfas to one-third that necessary for therapeutic response, pansulfa reduces the incidence of over-saturation and resulting renal damage. The combination of these three sulfonamides has in clinical practice an additive antibacterial effect.

Indications: Pneumococcic, streptococcic, meningococcic and staphylococcic infections, scarlet fever, rheumatic fever, erysipelas, otitis media, tonsilitis, urinary infections due to E. coli, Staphylococcus albus, Proteus and Pseudomonas.

Dosage: Adults—an initial dose of 8 teaspoonfuls, followed by 2 teaspoonfuls every 4 to 6 hours. Children—one teaspoonful for each 5 pounds of body weight per day, given in divided doses at four-hour intervals.

Supplier: The Wm. S. Merrell Company, Cincinnati, Ohio.

Roche-Organon Introduces Two New Hormone Products

Roche-Organon Inc. has just introduced to the medical profession two new hormone products. The first is neo-hombreol (M) sublingual tablets for buccal administration of male sex hormone therapy; the second new product is 25-mg. progestoral tablets for high-potency oral luteal therapy.

Neo-hombreol (M) sublingual tablets, each containing 5 mg. of pure methyl testosterone, are skillfully compounded for absorption through the mucous membrane of the mouth and provide a potent androgenic effect when placed beneath the tongue or between the gum and cheek and retained there until completely absorbed. Buccal therapy with Neo-hombreol (M) sublingual tablets is especially appreciated by patients when the swallowing of tablets is inconvenient, impossible or embarrassing as during travel or business hours. They are available for the physician's prescription in boxes of 30 and 100.

The new high-potency progestoral tablets, each containing 25 mg. of pregneninolone (anhydro-hydroxy-progesterone), are of particular value because of the recent trend toward larger doses of luteal hormone to assure results. They will be found especially useful in the treatment of functional uterine bleeding and threatened abortion. In view of the protracted character of many disorders responsive to luteal therapy, the convenience, as well as economy, of these high-potency progestoral tablets assumes

special significance. The new 25-mg. tablets are available in boxes of 20 and 100.

Schering Introduces High Potency Pranone Tablets

Due to the definite trend towards higher dosages of progesterone for the treatment of threatened and habitual abortion, Schering has added 25 mg. tablets of *pranone* to their endocrine line:

Pranone is anhydrohydroxy-progesterone, the effective oral form of the corpus luteum hormone. Progesterone has been found to be essential for the maintenance of pregnancy. With 25 mg. *pranone* tablets available to the patient at all times, minimizes the danger of abortion.

Used with exceptional success in the treatment of premenstrual tension, dysmenorrhea and functional uterine bleeding, the new higher potency tablet of *pranone* offers greater convenience and economy to the patient.

Johnson & Johnson Releases Hemo-Pak Hemostatic Absorbable Gauze and Cotton Dressings

Hemo-Pak hemostatic, absorbable surgical gauze and cotton, prepared from oxidized cellulose, effect hemostasis within two minutes after application to the bleeding points. The value of oxidized cellulose is based upon its properties of absorbability when buried in the tissues and its remarkable hemostatic effect without the cumbersome necessity of adding other hemostatic agents.

Absorption occurs between the second and seventh day following the implantation of the material, which is most effective when used dry. When exposed to blood, Hemo-Pak oxidized gauze or cotton turns black and forms a soft gelatinous mass which readily molds itself to irregular surface contours and controls hemorrhage by acting as a cork in the mouths of the bleeding vessels.

Hemo-Pak Gauze Packing Strips, 14″ x 2″, are particularly useful in general and urologic surgery small arterial hemorrhage under conditions when for the control of venous or capillary hemorrhage or suturing or ligation is impractical.

Hemo-Pak Gauze Packing Strips, ½″ x 2½ yds., are especially adapted to otolaryngological procedures. Their use provides a ready means of controlling stubborn or inaccessible bleeding and helps eliminate the usual foul condition in the nose observed when regular gauze packing is used. Disintegration of the material in body orifices is followed by absorption or spontaneous ejection.

Hemo-Pak Cotton Pads, 6″ x 2″, find a field of usefulness in neurologic surgery and ear, nose and throat procedures.

Aspogen—New Gastric Antacid

A new gastric antacid—*aspogen*—is announced by Eaton Laboratories. Aspogen is the Eaton brand of basic aluminum aminoacetate, the basic aluminum salt of the amino acid glycine. It is intended as an adjunct in the treatment of peptic ulcer and for the symptoms of hyperchlorhydria.

Aspogen has the advantage of both rapid and prolonged neutralization of gastric hydrochloric acid without producing constipation. The primary rapid action results from a combination of hydrochloric acid with the amino acid fraction of the molecule.

The secondary prolonged effect results from the reaction of more acid with the basic aluminum portion of the molecule. These can rapidly raise the reaction of hydrochloric acid toward pH 5. The gastric contents cannot become alkaline with a resulting rebound secretion of acid. No carbon dioxide is released during neutralization of the acid.

Clinical investigation reveals that this material is an effective and palatable method of treatment of peptic ulcer with a minimum amount of untoward side effects. It does not produce flatulence, eructation or constipation.

Aspogen is supplied in the form of soft palatable tablets of 0.5 Gm. each, sealed in cellophane tape in cartons of 100 and in bottles of 500.

Carfusin Rorer Now Council-Accepted

Carfusin *rorer* has been accepted for inclusion in *New and Nonofficial Remedies* by the Council on Pharmacy and Chemistry of the American Medical Association. Carfusin, produced by William H. Rorer, Inc., pharmaceutical manufacturer, is Rorer's brand of Carbol-Fuchsin paint, and was formerly known by the name of Castellani's Paint.

Most physicians and pharmacists know that Castellani's Paint has been in use for years as a favorite remedy for athlete's foot and other fungus infections. Its chief disadvantages as a prescription preparation have been its lack of stability on the shelf and the messiness attendant upon its mixing. In 1946, Rorer chemists succeeded in its stabilization. Since that time, Castellani's Paint *rorer* (now Carfusin) has been a favorite with the physician as an effective, stable preparation and with the pharmacist who dispenses it.

Carfusin is available in one fluidounce applicator-top bottles and in four fluidounce bottles.

* * *

About Laennec's prime, we find *Rayer's disease*, or *Xanthoma*. Pierre Francois Olive Rayer was born in 1793. He was an advanced worker in pathology, natural history, therapeutics, epidemology and diseases of the kidney. He was the first to differentiate acute from chronic eczema, and had a great influence on Erasmus Wilson. Rayer published studies of glanders, farcy, cheilitis exfoliativa and adenoma sebaceum. He died in 1867.

New Theory on Electrocardiography Tagged Zonal Interference

Through the presentation of three papers by Dr. Louis H. Nahum, associate professor of physiology, Yale, Dr. Hyman Chernoff, U. S. Public Health Service Fellow and Dr. William Kaufman, a new theory for interpreting electrocardiograms was forwarded. This theory is called, *zonal interference*, and is based on the concept that it is the interaction of opposite electrical forces from different zones of the heart which creates the electrocardiogram.

It has been known for some time that even in normal hearts, the heart will often skip a beat. The new theory can show where such skips originate.

The previously held concept of the nature of the electrocardiogram is known as the *cavity potential theory*. Its explanations for the wavy lines and curves of the electrocardiogram are based on the idea that the cavities of the heart are the first to receive electrical impulses. As they spread, from the cavities of the heart externally to the surface, differences appear on the electrocardiogram.

Dr. Nahum and his colleagues pointed out by means of a "geographic" chart the distinct zones of the heart and how they will be reflected in electrocardiograms.

The Yale investigators stated that this schematic map of the heart zones now makes it possible to chart the spread of heart excitation without opening the chest by surgery—the only previous accurate method known to science to determine the time of arrival of an electrical stimulus at various portions of the heart.

They found that when they compared their results with those obtained by previous investigators, who worked with an exposed heart, that this method gave identical results.

The research was conducted on animals who were fed oxygen during the entire procedure. The Yale investigators studied each portion of the heart to learn what it contributes to the electrocardiogram.

The normal heartbeat of a man is from 60 to 70 beats per minute and each heart beat gives a complete electrocardiogram.

The above research, in addition, has shown the exact manner in which the three body sources for creation of an electrocardiogram reflect the activity of the heart. These three sources are the right and left arms and the left leg.

Institute on Cancer Uniquely Presented By The University of Wisconsin

Information released by the Medical School at the University of Wisconsin, Madison, announced that the Institute on Cancer presented at that institution from March 22 to March 25 was one of the most intensive enterprises of its type to be held in this area of the country.

The Institute was jointly sponsored by the Medical School of the University, the Wisconsin Division of the American Cancer Society, The State Board of Health of Wisconsin, and the State Medical Society of Wisconsin, with participation by the State Laboratory of Hygiene and the McArdle Memorial Laboratory for Cancer Research.

Material presented included such subjects as the enzymatic control of cell growth, discussion and demonstration of the Papanicoloau technique, and tissue study and techniques. There was detailed study and discussion of malignant lesions of the genito-urinary tract, the gastro-intestinal tract, and the organs of the female pelvis. X-ray diagnosis, gastroscopy and bronchogram methods were demonstrated.

The final day of the Institute included a joint meeting with the Field Army of Wisconsin and embraced such material as the organization of a successful cancer detection center, plus discussing the newer diagnostic methods.

* * *

The futility of eponyms is again illustrated by two diseases known as *Jacquet's disease*, after Lucien Jacquet, 1860-1896. Reflex alopecia connected with anomalies of teeth, and dermatitis simples infantiles are the two diseases. Jacquet initiated the dermatologic service at Hopitaux St. Antoine, and under his direction it became second only to the St. Louis at Paris. Jacquet began the anti-alcohol campaign in France. He was joint editor of the *Precis Eleméntair*, and of the *Annales of Dermatology*.

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DIASTOLIC **Male	76.4	78.1	78.8	79.5	80.4	81.4	82.3	83.3	84.3	84.5	84.0
Female	75.8	77.1	78.0	78.6	79.9	81.9	83.9	85.4	86.8	86.8	84.4

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*Blood Pressure. Report of Joint Committee on Mortality of The Association of Life Insurance Medical Directors and The Actuarial Society of America. New York, 1925, pp. 10, 52.

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